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"IODIDE-MYXEDEMA" IN PATIENTS WITH CHRONIC CHEST DISEASE*

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It is well known that stable iodide inhibits thyroid function in Graves' disease.[1] Hypothyroidism has been observed in such cases after prolonged iodide treatment[2] as early as 1928. In recent years there have been several reports of myxedema induced by iodide therapy in patients who have never been hyperthyroid.[3-11] Three such cases of iodide-induced myxedema have been observed at Sunnybrook Hospital, Toronto. All of these patients had chronic bronchitis and emphysema and all had been taking iodide as medication. The clinical features of hypothyroidism regressed quickly once the ingestion of iodides was discontinued. It is the purpose of this paper to draw further attention to this reversible cause of myxedema that may easily be overlooked.

Case 1.—Mr. W.N., a 56-year-old carpenter, was admitted to Sunnybrook Hospital on December 17, 1956, complaining of severe fatigue and weakness. His only previous significant illness was chronic bronchitis and emphysema, for which he was pensioned. About one year prior to admission he noted that it was difficult for him to keep warm. Next, the skin of his hands became increasingly thick, and his hands felt stiff and clumsy. He lost much of his body hair including the eyebrows. For the first time in his life he had to use laxatives. Other complaints of recent onset were moderate deafness, hoarseness and thick tongue. By the time he was admitted he was hardly able to walk because of weakness and unsteadiness.

On examination he was pale but appeared well developed and well nourished. He spoke very slowly and took about one minute to subtract 7 from 100. His face was expressionless and his skin was dry, cold, roughened and thickened, especially over his extremities. The thyroid gland was palpable but not enlarged, tender or nodular. The lower lung borders expanded poorly and many rhonchi were heard bilaterally. His cardiac rate was 68 per minute and his blood pressure was 120/80 mm. Hg. There was marked generalized weakness but no muscular atrophy. The remainder of the examination contributed nothing pertinent to his problem.

Laboratory investigation revealed a hemoglobin of 70% with a normal smear and differential. His chest radiograph was not remarkable and showed a normal-sized heart. Barium meal examination showed decreased gastrointestinal motility. In the electrocardiogram there was low voltage and flat T waves suggestive of myxedema. His serum cholesterol was 185 mg. per 100 ml., and his basal metabolic rate was minus 15%. I^{131} uptake was less than 1% (normal 15-40%); the serum protein bound iodine was elevated to 10 micrograms per 100 ml. (normal range 3.5-6.5 micrograms (μg.) per 100 ml. in our laboratory).

Iodide-induced hypothyroidism was suggested because of the clinical features of myxedema associated with the high protein bound iodine. In the drawer of the patient's bedside table was found a box of Felsol powders. He had been taking this medication for at least 18 months as treatment for his chronic pulmonary disease. Felsol contains, among other ingredients, 30 mg. of iodopyrine in each cachet. The patient had been taking a total of 125 to 150 mg. of iodopyrine daily, irregularly and intermittently for 18 months. He improved rapidly on no other therapy than the withdrawal of iodides. The I^{131} uptake became greater than normal (52%). Changes in the other relevant laboratory data are listed in Table I. A heavy growth of hair reappeared on his face, trunk and extremities. His skin became warm and of a normal texture. By mid-February 1958, he was back to his normal state of good health.

Case 2.—Mr. S.H.B., aged 56, a Department of Veterans Affairs employee, was admitted to Sunnybrook Hospital on January 20, 1957, because of a sudden increase in shortness of breath. The diagnosis of chronic bronchitis with emphysema had been made in this man in 1945. In March 1956, he was treated in Sunnybrook Hospital for bacterial pneumonia. He was discharged later on ten minims of saturated solution of potassium iodide (each minim containing 1 grain of potassium iodide) three times a day, as well as other medications.

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TABLE I.—SUMMARY OF RELEVANT LABORATORY DATA IN PATIENT W.N., AGED 56 (CASE 1)

Date	*24 hr. thyroid uptake of* I^{131} *(%)**	*Serum PBI†* *(μg./100 ml.)*	*B.M.R.*	*ECG*
1956 Dec. 21	0			Low T waves
Dec. 22		*Iodide discontinued*		
Dec. 26		10.0		
1957 Jan. 15			−15%	
Jan. 22	52	7.0		
Jan. 25			+1%	T waves
Jan. 29		6.2		better
Feb. 9	34			formed
Feb. 12		5.5	+15%	

*Normal range: 12-40%.
†Normal range: 3.5–6.5 μg./100 ml. (by modification of the method of Barker.[11]

By October 1956, he was complaining of increasing lethargy and easy fatigability. His eyelids had become puffy, and this change interfered with proper fitting of his glasses. There was a steady decrease in exercise tolerance over the next two months. He was readmitted to Sunnybrook Hospital in December 1956, because of shortness of breath and an episode of hemoptysis.

On examination he was a well-developed, well-nourished, pale man with puffy eyelids, appearing about 10 years older than his stated age of 56. His skin was dry and flaking, his voice was hoarse, and he was moderately deaf. The thyroid gland was not palpable. The lungs were emphysematous. His blood pressure was 140/100 mm. Hg and his cardiac rate was 80 per minute. He performed simple calculations very slowly and his tendon reflexes were slow to relax. Chest roentgenograms showed changes compatible with emphysema.

Because he appeared somewhat hypothyroid, an I^{131} uptake was done and found to be 2%. This reading was thought to be fallacious because the patient had been on potassium iodide medication. A protein bound iodine estimation was not done at this time. No cause was found for the patient's hemoptysis. He became less dyspneic and was discharged on January 18 without drug treatment.

Five days later, on January 23, 1957, the patient was readmitted because of sudden onset of acute dyspnea, followed shortly afterwards by the signs of profound shock. An electrocardiogram was compatible with acute anterior myocardial infarction. On supportive measures he gradually improved. The blood pressure returned to 160/100 mm. Hg in the next 24 hours. He was treated with rest in bed for six weeks, and was kept in hospital for control of anticoagulant therapy. The medication containing iodide was not given during this admission.

By the end of January, four weeks after the iodide was stopped, it was noted that the patient was feeling stronger and more energetic. By mid-February his skin was soft and pliable, his voice was no longer hoarse, and he could walk normally with a steady gait. He could hear well and he was able to perform mental arithmetic quickly. The swelling of his eyelids had disappeared and the tendon reflexes had become normal. He felt warmer and sometimes sweated. The important laboratory findings are summarized in Table II.

TABLE II.—SUMMARY OF THYROID FUNCTION TESTS IN PATIENT S.B., AGED 56 (CASE 2)

Date	*24-hr. thyroid uptake of* I^{131}	*Serum PBI (μg./100 ml.)*	*Clinical*
27/12/56	2%	—	Hypothyroid
4/1/57		*Iodide discontinued*	
30/1/57	48%	10.5	
9/2/57	26%		
18/2/57		7.4	Euthyroid

On February 24 he suddenly became short of breath and went rapidly into shock with acute pulmonary edema from which he died a few hours later.

At autopsy the lungs had the changes appropriate to chronic bronchitis, emphysema and pulmonary edema. There was marked arteriosclerotic thickening of the coronary arteries with a recent, partially organized infarct superimposed on an area of old infarction in the anterior wall of the left ventricle and septum near the apex. There was dilatation of all chambers of the heart, with right-sided hypertrophy. The thyroid gland weighed 15 g. The right lobe was twice as large as the left. The cut surface was finely lobulated but no nodules were seen. Microscopically there was an increase in the interstitial connective tissue with an accentuation of the lobular pattern. There were intraluminal projections in a few medium-sized follicles.

The adenohypophysis was not enlarged. It had a normal appearance on histological examination.

CASE 3.—Mr. J.S., aged 58, was a former taxi driver who had several previous admissions to Christie Street and Sunnybrook Department of Veterans Affairs Hospitals for treatment of duodenal ulcer. In 1951, after an episode of gross hematemesis, he underwent a subtotal gastrectomy. During his convalescence this patient suffered a myocardial infarction. Thereafter he had angina pectoris on moderate exertion.

For two years he had difficulty in walking because of incoordination in his lower limbs. After neurological investigation, the additional diagnoses of spontaneous cerebellar degeneration and psychopathic personality were made. He also had chronic bronchitis and emphysema.

On December 26, 1956, he was seen at the Eye Clinic with chronic glaucoma and acute blepharoconjunctivitis. Because he was no longer able to look after himself at home, he was admitted for treatment and domiciliary care. At that time he had no symptoms or signs of hypothyroidism. For chronic cough the patient was given mistura expectorans sed. (which contains 6 grains of potassium iodide in each fluid ounce), 8 c.c. four times a day from January 31, 1957, to June 12, 1957. By June he had developed obvious myxedema. The skin under his eyes hung in redundant folds. His voice was hoarse and his skin was very dry. By this time he was complaining of feeling cold.

Laboratory studies confirmed the diagnosis of iodide-induced myxedema; these are listed in Table III. When treatment by mist. expect. was discontinued he improved rapidly except that for a few weeks he suffered from more frequent attacks of angina than usual. By mid-August he showed no clinical evidence of thyroid dysfunction.

TABLE III.—SUMMARY OF RELEVANT LABORATORY DATA OF PATIENT J.S., AGED 58 (CASE 3)

Date	*24-hr. thyroid uptake of* I^{131}	*Serum PBI (μg./100 ml.)*	*B.M.R. (%)*	*ECG*
1957 June 7	1	17.4		Low voltage
June 8		*Iodide discontinued*		
June 20	63	9.5		
July 11		8.2		
July 17			−18	
Aug. 21	34	5.4	− 9	T waves better formed
Sep. 12		4.7		

DISCUSSION

In all of our cases the 24-hour uptake of I^{131} by the thyroid gland was low when the patients first presented with hypothyroidism. Then for a time, early in the period of recovery, the 24-hour uptake of I^{131} became greater than normal. This rebound phenomenon is characteristic of temporary hypothyroidism induced by an antithyroid drug and appears to be mediated by excessive circulating thyrotrophin (thyroid stimulating hormone or TSH) acting on the "unblocked" thyroid gland.

In myxedema, the lack of circulating thyroid hormone allows an increased production and release of thyrotrophin that normally would be somewhat inhibited by thyroid secretion. When the thyroid gland recovers sufficiently to put out normal quantities of thyroid hormone, the level of TSH falls and the I^{131} uptake returns to the normal range.

The occurrence of goitre, which has been reported in some cases of iodide-myxedema (but which was not observed in any of our cases), could also be explained as an effect of TSH acting on a "blocked" thyroid gland, which is still able to hypertrophy. According to these other case reports the enlarged thyroid gland became smaller following the withdrawal of iodide.

The serum protein-bound iodine (PBI) usually measures the amount of circulating thyroxine, but other iodine-containing material can adhere to the precipitated serum protein and resist the washing usually applied. Accordingly, fallaciously high values for PBI will result. The serum PBI values in our patients were elevated because of iodine contamination. The presence of clinical myxedema makes it certain that the circulating level of thyroid hormone was greatly reduced. Butanol extraction of the serum, and subsequent washing with alkali, usually frees the thyroxine fraction of inorganic iodide. However, this technique was not applied to the serum of any of our patients.

The site of the inhibitory action of iodide ion on thyroid function has been the subject of several studies. In the syndrome of iodide-myxedema, the I^{131} is accumulated in the recovery period as inorganic iodide and it can be discharged by perchlorate or thiocyanate.[9] This suggests that there is a block in organic iodination. Iodides inhibit the release of thyroid hormone from the gland in patients with Graves' disease, but it seems unlikely that a similar effect is present to an important degree in iodide-induced hypothyroidism. Inhibition of release would not account for the observation that much I^{131} is not organically bound at the time of the elevated I^{131} uptake.

Most articles on this subject contain a comment concerning the rarity of this condition in view of the extensive use of iodides in medical treatment. The most widely held view is that long duration and regularity of ingestion of iodide must be combined with some increased susceptibility to the disorder, perhaps because of an unrecognized mild defect in the synthesis of thyroid hormone, either inborn or acquired.

In patients with myxedema who have been taking iodides, a repeat radioiodine uptake a few weeks after withdrawal of iodide will establish this diagnosis. If the ingestion of iodide is at fault, the spontaneous elimination of part of it will then permit the trapping of I^{131}. The "count" over the thyroid should be done at four hours, as well as at 24 hours, because loosely bound I^{131} may be "flushed" at four hours with sodium thiocyanate or potassium perchlorate. The earlier determination provides additional evidence of a disturbance in organic binding. This "flushing test" has been described elsewhere.[10] Although this disease is rare, hypothyroidism should be remembered as a possible cause of debility in patients with chronic bronchitis and emphysema who are receiving long-term iodide treatment.

SUMMARY

Three cases of iodide-induced, temporary myxedema observed at Sunnybrook Hospital, Toronto, are reported. All had chronic pulmonary disease for which they were receiving iodide-containing medication. The possible mechanisms involved are discussed.

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PARA-INFLUENZA VIRUSES IN ASSOCIATION WITH ACUTE LARYNGOTRACHEOBRONCHITIS, TORONTO, 1960-61*

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ALTHOUGH the number of patients admitted to The Hospital for Sick Children, Toronto, with the syndrome of acute laryngotracheobronchitis (tracheitis) has increased steadily from 267 in 1953 to 615 in 1958, and despite a negligible mortality rate due to the institution of active therapeutic measures such as sedation and moist oxygen in a special tracheitis ward, the etiology of this condition in Toronto children has remained relatively obscure. The tracheitis syndrome comprises coryza, croupy cough, inspiratory stridor and dyspnea often accompanied by a hoarse voice or cry, indrawing of the thoraco-abdominal wall around the rib cage and fever ranging between 99 and 104° F. Although cases have occurred during all months of the year, characteristically the incidence of tracheitis is highest between November and March.[1-3] While children of all ages are affected, tracheitis was encountered most frequently in children between 12 and 23 months of age during the 1952-53 and 1953-54 winters.[3]

In Toronto during the winter of 1953-54, the isolation of agents—cytopathic both for trypsinized monkey kidney tissue cultures and explant cultures of human embryo lung fibroblasts—from material obtained by tracheal suctioning from five of 21 patients who required tracheotomy[2] strongly suggested that viruses, apart from well-known agents such as measles, varicella and influenza, may be etiological agents in the tracheitis syndrome. During the winter of 1955-56 strains of virus now termed Para-influenza-2 were isolated—from material from tracheal suctioning obtained from five of seven patients and nasopharyngeal suctioning from five of eight patients with tracheitis in Toronto—by inoculation of human amnion, monkey kidney or HeLa cells.[4] Rising Para-influenza-2 antibody titres in sera from six Toronto patients confirmed that infection was due to this virus. During the same winter in Cincinnati, strains of Para-influenza-2 virus, termed initially C.A. (croup associated) virus, were recovered from pharyngeal swabs taken from two of 12 infants with croup,[5] and rising antibody titres to this virus were found in paired sera from four patients, two of whom yielded virus. In Kent, England, Para-influenza-2 virus was isolated from throat swabs obtained from two of five children with tracheitis, and rising antibody titres to this virus were detected in paired sera from two patients, one of whom excreted virus.[6]

For the first time, Para-influenza-1 and Para-influenza-3 viruses were found frequently in association with a variety of respiratory illnesses in Washington, D.C., during 1957.[7] These viruses were termed initially H.A.-2 and H.A.-1 respectively, since tissue cultures infected with these agents showed the hemadsorption phenomenon.[8] Because of the close antigenic relationship between H.A.-2 virus and Sendai virus,[9] which was first isolated in Japan from lungs of newborn infants who developed pneumonitis,[10] the term *Myxovirus para-influenzae-1* (Para-influenza-1 virus) has been designated to include strains both of H.A.-2 and Sendai virus.[11] Between October 1957 and September 1958, 47 of 830 infants and children who were admitted to a Washington, D.C., hospital with respiratory infections had croup.[12] Isolation of Para-influenza-1 virus from 12 patients and rising titres of complement fixing antibody to this agent in sera from 15 patients confirmed that this virus frequently caused infection during an attack of croup, whereas Para-influenza-2, Para-influenza-3 and the Adenoviruses were isolated from croup patients infrequently. The isolation of Para-influenza-1 and Para-influenza-3 viruses from children with croup in Melbourne, Australia,[13] of Para-influenza-1 virus from children with respiratory tract infections in London, England,[14] and of Para-influenza-3 virus from military personnel who had influenza-like disease in California,[15] together with the demonstration of rising antibody titres to Para-influenza-1 or Para-influenza-3 viruses in Wisconsin students,[16] adults and children in England[17] and Scotland,[18] and children in Winnipeg,[19] has shown that these viruses are associated with acute respiratory infections, especially of children but also of adults, in many parts of the world.

The present paper reports the results of virus isolations, antibody studies and bacteriological investigations on 155 Toronto children who developed acute laryngotracheobronchitis with croup, between November 1960 and January 1961.

METHODS AND MATERIALS

Samples of nasopharyngeal secretions for bacteriological and virological examination were obtained from all patients by the Auger[20] suction technique. Specimens were examined bacteriologically the same day. When it was not possible to conduct virological tests the same day, the secretions were held at –20° C. for periods not exceeding one week.

Secretions from each patient were examined for bacteria by streaking on plates of blood agar and Levinthal agar. Organisms which gave rise to colonies morphologically typical of those produced by human pathogens were identified positively by appropriate biochemical and serological tests.

For virological tests, secretions were dispersed in 5 ml. of Hanks' balanced salt solution. After

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centrifugation at 8000 R.P.M. for 30 minutes in a Spinco model L centrifuge in order to deposit bacteria, 1-ml. aliquots of the supernatant fluid were inoculated into each of four drained roller tubes containing monolayers of monkey kidney epithelial cells. The tubes were rolled for one hour at 37° C., after which the fluid was removed by means of a pipette and replaced by 1 ml. ELY maintenance medium (Earle's balanced salt solution containing lactalbumin hydrolysate 0.5%, yeast extract 0.1%, penicillin 1000 units per ml. and streptomycin 500 μg. per ml.). The tubes were incubated on roller drums at 37° C. for periods up to 12 days. Usually on the fourth, seventh and twelfth days after inoculation the tissue culture fluids from each of four tubes inoculated with the same specimen were removed and pooled. A sterile 0.1% suspension of guinea pig erythrocytes in physiological saline was introduced into each tissue culture tube and all tubes were examined microscopically for evidence of hemadsorption.[8] Usually eight uninoculated monkey kidney culture tubes from the same batch were treated identically as controls. When no hemadsorption was observed in control culture tubes, fluids from inoculated tubes in which hemadsorption was observed were examined for hemagglutination in the presence of a 1% suspension of guinea pig erythrocytes, using plastic plates and 0.2-ml. aliquots of virus dilutions similar to those described for mumps.[21] Fluids which had hemagglutinin titres of 8 or greater were typed as follows: Dilutions of antisera prepared in guinea pigs against Para-influenza viruses types 1, 2 and 3 containing four antibody units per 0.2 ml. were mixed with 0.2-ml. aliquots of freshly isolated virus diluted to contain four agglutinating doses. After 10 minutes' incubation at room temperature, 0.2-ml. aliquots of a 1% suspension of guinea pig erythrocytes were added to each serum-virus mixture. Inhibition of hemagglutination by Para-influenza-1 antiserum, but hemagglutination in the presence of antisera to Para-influenza viruses types 2 and 3, showed that the fresh isolate was a strain of Para-influenza-1 virus. Tissue culture fluids which contained fresh virus isolates were stored at –70° C.

Acute-phase and convalescent-phase sera were collected from 24 patients, 23 of whom yielded a Para-influenza virus at the time of illness. Unheated sera were examined for neutralizing antibody content to 100 TCD_{50} of the prototype strain of Para-influenza virus of the same antigenic type as that which was isolated from the patient, using two monkey kidney culture tubes per fivefold dilution.[22] Paired sera were also examined for antihemagglutinin content against four agglutinating doses of Para-influenza viruses types 1, 2 and 3 and mumps, after heating at 56° C. for 30 minutes and treatment with M/100 potassium periodate, as described previously for mumps virus.[21]

RESULTS

Virological and bacteriological studies were undertaken on 155 patients who were admitted to The Hospital for Sick Children with acute laryngotracheobronchitis (tracheitis) between November 1, 1960, and January 28, 1961. One patient, S.M., aged 11 months at the time of first admission with tracheitis, was readmitted one month later with the same condition. Since he showed serological evidence of infection with Para-influenza-3 virus at the time of his first illness, and Para-influenza-1 virus was isolated from his nasopharynx during his second illness, each illness is considered separately in this series of cases.

Most patients in this series exhibited the typical syndrome of acute laryngotracheobronchitis[1, 2] with croupy cough, hoarse voice or cry, respiratory difficulty especially on inspiration and indrawing of the chest wall in the subcostal, intercostal or supraclavicular areas. Cyanosis was uncommon. Although inspiratory rhonchi were heard frequently throughout the lung fields, no rales were heard on auscultation. Frequently the throat was injected but the epiglottis when visualized was not grossly reddened or swollen, except in one patient who presented with a precipitous onset of acute respiratory obstruction due to epiglottitis. Para-influenza-1 virus was isolated from the bronchial secretions of this patient, but *Hemophilus influenzae* type B was not isolated. Tracheotomy was performed on eight patients who had severe respiratory obstruction at the time of admission to hospital.

In 82 patients, croup was noted 12 hours or less prior to hospitalization, including 22 patients who had croup for three hours or less. In 37 patients croup lasted 13 to 24 hours and in 38 patients it was present for one to three days before admission. Symptoms, described loosely as a "cold", comprising cough, running nose and possibly slight fever, were observed in 63 patients before croup occurred; 54 of these had coryza-like symptoms two days or more before hospitalization.

TABLE I.—VIRUS ISOLATIONS AND ANTIBODY STUDIES IN 155 PATIENTS WITH ACUTE LARYNGOTRACHEOBRONCHITIS

		Rising or elevated antibody titres			
	Virus isolations	*AHA and NT*	*AHA only*	*NT only*	*No antibody*
Para-influenza 1	73	8	2	7	3
Para-influenza 3	7	3	0	0	0
Total positive	80				
Total tested	156				

AHA: antihemagglutinin test.
NT: neutralization test.

Para-influenza viruses were isolated from nasopharyngeal or tracheal secretions from 80 of 156 samples obtained from 155 patients (Table I). Of these, 73 strains were typed as Para-influenza-1 virus and seven were strains of Para-influenza-3

TABLE II.—ANTIBODY RESPONSES IN 23 PATIENTS WHO PROVIDED PAIRED SERA

Patient	Age	Onset of croup	Days in hospital	Virus isolation		Antibody titres Antihemagglutinin					Neutralization	
				day	type	day	P1	P2	P3	Mu	P1	P3
						2	0	0	0	—	0	—
S.H.	3 years	1/11/60	6	2	P1	18	0	0	0	—	50	—
						1	0	0	0	0	0	—
K.T.*	4 years	18/11/60	4	1	P1	69	20	0	0	40+	20	—
						4	0	0	0	—	—	20
J.L.	3 years	24/11/60	3	2	P3	21	0	0	20	—	—	250
						2	0	0	20	—	0	250+
S.B.	2 years	27/11/60	2	1	P3	20	0	40	40	—	—	250+
						3	0	0	0	—	—	20
L.B.	14 months	28/11/60	4	1	P3	18	0	0	40	—	—	250+
						3	0	0	40+	0	0	—
C.C.	2 years	3/12/60	3	2	P1	63	40+	0	40+	0	20	—
						5	0	0	0	0	0	—
L.F.†	9 months	7/12/60	12	2	P1	14	40+	0	0	0	20	—
						1	0	0	0	0	0	—
P.J.	2 years	11/12/60	2	1	P1	34	40	0	0	0	50	—
						8	0	40	40	0	0	—
C.D.‡	7 years	13/12/60	9	0	P1	32	0	40	40	0	20	—
						3	0	5	20	0	0	—
G.H.	2 years	14/12/60	2	2	P1	52	0	40+	20	0	0	—
						4	0	0	0	0	0	—
P.S.	2 years	17/12/60	3	3	P1	49	40+	0	0	0	50	—
						4	0	0	0	0	0	—
B.P.	18 months	19/12/60	4	3	P1	39	0	0	0	0	250	—
						2	0	0	40	0	20	—
T.F.	5 years	20/12/60	3	0	P1	36	5	0	40	0	20	—
						2	0	0	0	40+	0	—
D.K.	4 years	20/12/60	2	1	P1	24	0	0	0	40+	0	—
						2	0	0	0	40	0	—
W.W.	8 years	24/12/60	3	2	P1	21	0	0	0	40	250	—
						5	0	0	0	0	0	—
J.M.	2 years	24/12/60	2	4	P1	42	0	0	0	0	0	—
						3	0	0	40+	40	0	—
D.M.	2 years	27/12/60	4	2	P1	29	40+	0	40+	40	20	—
						2	0	0	0	0	0	—
G.R.	3 years	28/12/60	3	1	P1	31	0	0	0	0	250	—
						3	0	0	40+	0	0	—
R.F.	2 years	31/12/60	3	1	P1	35	40+	0	40+	0	20	—
						2	0	40	0	0	10	—
F.M.	4 years	3/1/61	3	1	P1	24	0	40	0	0	250	—
						2	0	0	0	0	0	—
H.C.	4 years	5/1/61	3	1	P1	43	0	0	0	0	50	—
						4	0	0	40+	0	0	—
J.K.‡	3 years	5/1/61	7	3	P1	11	5	0	40+	0	0	—
						2	0	0	10	0	0	—
S.K.	4 years	24/1/61	2	1	P1	18	10	0	20	0	0	—

*Had clinical mumps two weeks after tracheitis.

†Illness complicated by pneumonia.

‡Tracheotomy performed.

P1 = Para-influenza 1 virus; P3 = Para-influenza 3 virus.

— Not tested.

virus. Of the eight patients who required tracheotomy at the time of admission to hospital, tracheal secretions from five patients yielded Para-influenza-1 virus; no virus was recovered from the other three.

Acute phase and convalescent phase sera were obtained from 23 patients from whom a Para-influenza virus was isolated, including 20 who excreted Para-influenza-1 virus and three who yielded Para-influenza-3 virus (Table II). Amongst the Para-influenza-1 virus excretors, eight patients showed rising or elevated antibody titres to the prototype strain of Para-influenza-1 virus both in antihemagglutinin and neutralization tests, two patients showed serological evidence of infection on antihemagglutinin tests only, in seven patients rising or elevated titres were detected by neutralization only, and three patients showed no antibody by either test. Serological evidence of infection with Para-influenza-3 virus was detected in all three excretors of this virus who donated paired sera. Elevated levels of Para-influenza-3 antihemagglutinin were detected both in acute and convalescent phase sera from eight patients who had Para-influenza-1 virus infections. Para-influenza-2 antihemagglutinin was detected in acute and convalescent phase sera from two patients infected with Para-influenza-1 virus (Table II). Rising titres of Para-influenza-2 antihemagglutinin were observed in two patients, one of whom had a Para-influenza-1 virus infection (G.H.) while the other (S.B.) was infected with Para-influenza-3 virus.

In view of several reports that infection with Para-influenza-1 virus may stimulate rising antibody titres both to this virus and mumps,[16] or that an attack of mumps may evoke rising antibody

TABLE III.—ANTIBODY RESPONSE TO INFECTION WITH PARA-INFLUENZA-1 AND MUMPS VIRUSES

Infecting virus	*No. of patients*	*Age*		*Rising antihemagglutinin titres*	
		5 yrs. or less	*6 to 11 years*	*Para-influenza-1*	*Mumps*
Para-influenza-1	19	17	2	10	1*
Mumps	20	7	13	0	20

*This patient had clinical mumps during convalescence from Para-influenza-1 virus infection.

titres both to mumps and Para-influenza-1 virus,[19, 23, 24] paired sera from 19 Para-influenza-1 virus excretors were tested for antihemagglutinins to the G.M. strain of mumps virus which was isolated during 1960 by inoculation of monkey kidney tissue cultures with cerebrospinal fluid of a patient who had mumps meningoencephalitis.[21] A rising titre of mumps antihemagglutinin was detected in one patient (K.T.) who developed clinically typical mumps two weeks after the onset of tracheitis due to infection with Para-influenza-1 virus. This patient also showed rising antihemagglutinin and neutralizing antibody titres to Para-influenza-1 virus (Table II). Elevated mumps antihemagglutinin titres were detected in sera of three other patients, one of whom did not develop Para-influenza-1 antibody and two of whom showed rising levels of Para-influenza-1 antibody in antihemagglutinin and/or neutralization tests. Mumps antibody was not detected in sera of the other 15 patients (Table III). Furthermore, paired sera from 20 patients who had rising mumps antihemagglutinin titres following mumps meningoencephalitis during 1960[21] were tested for antihemagglutinin levels to Para-influenza-1 virus. Antibody to Para-influenza-1 virus was detected in sera from one patient only and the titre remained constant during convalescence.

The peak incidence of admissions to hospital with croup occurred during the first week of January 1961. Para-influenza-1 virus was isolated from 15 of 22 patients admitted during that week (Table IV). The maximum incidence of isolation of Para-influenza-1 virus occurred during the last two weeks of December and the first fortnight of January. Most infections with Para-influenza-3 virus occurred during late November and early December, after which the incidence of Para-influenza-1 virus infections increased profoundly.

Para-influenza-1 virus was isolated from 52 of 102 patients during the first three years of life (Table V). The isolation rate of Para-influenza-1 virus in children who had passed their third birthday was more variable.

Bacterial cultures were done on 132 of the 155 samples of nasopharyngeal secretions, 64 of which yielded a Para-influenza virus and 68 of which did not. It was impossible to assess the significance of the bacteriological findings because no consistent pattern emerged and because studies of the serological responses in individual patients to the potential bacterial pathogens were not made.

TABLE IV.—WEEKLY INCIDENCE OF ISOLATIONS OF PARA-INFLUENZA VIRUSES IN PATIENTS WITH TRACHEITIS

Month	*November*				*December*					*January*				*Totals*
Week number	*44*	*45*	*46*	*47*	*48*	*49*	*50*	*51*	*52*	*1*	*2*	*3*	*4*	
Para-influenza 1	2	0	3	1	4	6	12	11	8	15	6	2	3	73
Para-influenza 3	0	0	0	2	4	0	0	0	1	0	0	0	0	7
Specimens tested	13	1	6	9	17	10	14	20	19	22	10	5	10	156

In 23 cases, the cultures failed to yield growth, presumably because of the use of antibiotics; in another 48 cases only normal pharyngeal flora were found. These findings were equally distributed between those cases with virus (36 instances) and those without (35 instances). Potentially pathogenic bacteria were found in the remaining 61 cases, sometimes in combination. Again these were distributed almost equally between those patients with virus and those without. Thus pneumococci were found in 15 of the group with virus and in 11 of those without; *Hemophilus influenzae* was found in 11 of those with and 11 of those without virus; staphylococci were present in eight of the virus-positive cases and in 15 of the virus-negative ones. A hemolytic streptococcus that proved non-groupable was isolated once. None of the strains of *H. influenzae* were type B. Suitable antisera for determining other types or for typing the pneumococci were not available.

TABLE V.—INCIDENCE OF PARA-INFLUENZA VIRUS ISOLATIONS IN VARIOUS AGE GROUPS

	Under 12 months	*12-23 months*	*24-35 months*	*36-47 months*	*4 and 5 years*	*6 or more years*
Para-influenza 1	11	18	23	8	9	4
Para-influenza 3	1	1	2	1	0	2
No virus	12	17	17	13	8	9
Total tested	24	36	42	22	17	15

DISCUSSION

The high rate of isolation of Para-influenza-1 virus from the respiratory tracts of Toronto children who developed acute laryngotracheobronchitis during the winter of 1960-61, together with serological evidence of infection in 17 of 20 patients whose sputa yielded Para-influenza-1 virus, points strongly to an etiological association between this virus and tracheitis. Virological or serological evidence of infection with this virus has been demonstrated repeatedly in children with tracheitis[12, 13] or other respiratory infections.[7, 9, 14, 23] Although Para-influenza-3 virus was associated with relatively few cases of tracheitis in the present series, it has been associated with outbreaks of acute respiratory disease[7, 13-15] in both children and adults. Para-influenza-2 virus, which was not isolated during the present study, has less commonly been associated with outbreaks of croup.[4-6]

In Toronto children, infection with Para-influenza-1 virus was not followed by rising titres of mumps antihemagglutinin. These findings and similar observations in Winnipeg children[19] are in contradistinction to the demonstration by Gardner[17] of a rising mumps antibody titre following Para-influenza-1 infection in a man aged 20 years. Similarly the lack of production of Para-influenza-1 antihemagglutinin following infection with mumps virus in Toronto children contrasts sharply with the demonstration of rising Para-influenza-1 antibody levels in sera from 21 of 24 young adults in Wisconsin,[24] in five of nine children in Winnipeg[19] who had mumps and in 35 of 66 mumps patients from central England.[23] Using hyperimmune guinea pig sera, a potent mumps antiserum bound complement at low titre in the presence of Para-influenza-1 soluble antigen,[10] but no cross-reactions were demonstrated between mumps and Para-influenza-1 viruses in complement fixation tests using the virus particle antigen, or in antihemagglutinin tests. The lack of heterologous reactions to mumps or Para-influenza-1 viruses in antihemagglutinin tests with sera of Toronto children may be due either to the higher degree of antigenic specificity of this test in comparison to the complement fixation test which most other workers have used or to the fact that this was the first myxovirus infection which these children had encountered. It is possible that repeated myxovirus infections may broaden the antibody response to a particular myxovirus.

In sera from 37 Washington, D.C., children who had rising Para-influenza-1 antibody titres, neutralization and antihemagglutinin tests were almost equally efficient in detecting this antibody increment.[25] However, in 20 Toronto patients from whom Para-influenza-1 virus was isolated, serological evidence was detected by the antihemagglutinin test in 10 patients only, but neutralization tests gave positive results in seven further patients. Use of both antihemagglutinin and neutralization tests in the diagnosis of Para-influenza-1 infections therefore seems desirable.

SUMMARY

Between November 1, 1960, and January 28, 1961, virological and bacteriological studies were carried out on 155 children, including 60 under two years of age, who were hospitalized with acute laryngotracheobronchitis. Isolation of Para-influenza-1 virus from 73 children, 17 of whom showed serological evidence of infection with Para-influenza-1 virus, and isolation of Para-influenza-3 virus from seven children, together with serological evidence of infection in three of these, suggested strongly an etiological association between these viruses and tracheitis.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

Typhoid fever has been almost a constant factor in the monthly mortality returns of the city of Ottawa for several years past, but at no period, up to the end of 1910, was there any marked increase in the number of deaths reported. During the past ten years, 1901-1910, 200 deaths have been reported, and of these 38 died in 1907 and 6 in 1903, the years of greatest and least mortality from the disease. The average was 20 deaths a year. In 1910 the mortality was 24. Up to March 18th, 1911, the date at which the investigation closed, in a period of eleven weeks there were 52 deaths for 1911.

The incidence of this disease during the past ten years cannot be ascertained owing to the obvious incompleteness of the official returns. For instance, in the year 1909, only 58 cases were reported, while 23 deaths were recorded. In 1910, 80 cases were reported with 24 deaths. Obviously this mortality is incredibly high for the number of cases, and one is justified in concluding that during these years and the preceding ones, many cases of typhoid fever have occurred in the city unreported.—L. Drum, Typhoid Fever at Ottawa, *Canad. M. A. J.*, 1: 731, 1911.

A PRELIMINARY REPORT OF THE ANTI-INFLAMMATORY EFFECT OF OXYPHENBUTAZONE (G27202) IN POSTOPERATIVE OBSTETRICAL AND GYNECOLOGICAL PRACTICE*

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INFLAMMATORY disease, and the destructive process that follows in the wake of its resolution, have been the anathema of the surgeon for many years. The poor clinical results of many forms of current therapy provide the physician with a constant stimulus to seek out new pharmaceutical tools in an effort to find some sound means of modifying the tissue reaction to injury so that organs involved in reparative processes may resume their normal physiological function.

One drug shown to possess anti-inflammatory properties is phenylbutazone (Butazolidin). Unfortunately, the use of this drug has been complicated by the onset of serious side effects in a certain percentage of cases, and the drug, although active and efficient, is used with every caution because of the potential hazard to the patient.

Investigation of the pharmacology of phenylbutazone proved that it was metabolized slowly in man and that it appeared in two altered forms in human urine: Metabolite I or 1-phenyl-2-(p.hydroxyphenyl)-3-5-dioxo-4-n-butyl pyrazolidine, and Metabolite II or 1,2 diphenyl-4-(γ-hyroxy-n-butyl)-pyrazolidine-3,5-dione. Metabolite I, otherwise known in recent clinical trials as G27202,† oxyphenbutazone or Tandearil,† has been used experimentally on inflammatory lesions in animals and was noted to have the following effects: (a) a lower toxic median lethal dose; (b) less irritating effect on the gastric mucosa of animals[1]; and (c) a markedly stronger antipyretic property and an identical anti-inflammatory activity[2] when compared to the parent compound.

Several papers recently published[3-7] describe the anti-inflammatory action of the drug G27202 in man, with few side effects in the dosage prescribed.

In an effort to evaluate this drug clinically, the following experiment was set up in the obstetric and gynecological wards of the Royal Victoria Montreal Maternity Hospital.

MATERIALS AND METHODS

A double blind study was inaugurated in the following manner:

G27202 was kindly supplied by Geigy Pharmaceuticals in the form of small white sugar-coated pills containing 100 mg. of the active ingredient per tablet.

A placebo pill of exactly the same dimensions, colour and weight was also made available.

The tablets were divided into lots of 100 and placed in bottles with no other marking than a single numeral. The bottles were then given to the ward charge nurse who allotted the tablets from numbered bottles to two equal groups of patients on opposite sides of the ward. Unknown to any of the clinical investigators, the contents of the numbered bottles were changed from placebo to G27202 and vice versa at intervals, to minimize the chance of "clinical impressions" being formed by those of us who saw the patients regularly.

After completion of the individual course of therapy, the ward charge nurse placed the correct bottle number on the patient's progress sheet. Subsequently the data were summarized and transferred to punch cards which were, after completion, labelled "Placebo" or "G27202" by a fourth individual. The investigators had no knowledge of which patient was given either form of therapy during the hospital admission.

All obstetrical cases requiring episiotomy, repair of third-degree tears, deep vaginal tears and Cesarean section were included in the series.

Patients subjected to gynecological procedures, including abdominal operations, vaginal hysterectomies, repair of sacro-pubic hernias and vulvectomies, were also included in the series.

Because of the known salt-retaining tendency of the drug, patients with a history of toxemia, nephritis, hypertension or heart disease were not studied. All patients over the age of 60 years were arbitrarily excluded from the study.

DOSAGE AND ADMINISTRATION

Since the pathway of excretion of the drug in the pregnant human is unknown, the drug was administered post partum only, but was supplied to both nursing and non-nursing mothers. A loading dose of 400 mg. for 24 hours followed by 300 mg. daily in divided doses was given to all patients.

Gynecological patients were given 400 mg. in divided doses 24 hours prior to operation where practicable. Patients undergoing emergency procedures were given a 400 mg. loading dose in the 24 hours postoperatively followed by 300 mg. in divided doses daily thereafter. The tablets were given by mouth, accompanied by a glass of water.

ASSESSMENT OF THE PATIENT

An attempt was made to see each patient daily during the study. It is obvious that an unbiased assessment of the degree of relief of pain is extremely difficult clinically, because of the variability of pain threshold, the reaction of different racial groups, and language barriers. Such an assessment was attempted, based partially on described subjective symptoms and partially on the patient's demand for other forms of analgesia.

*From the Royal Victoria Montreal Maternity Hospital and McGill University, Montreal.
†Geigy Pharmaceuticals (Canada) Limited.

The objective signs of local erythema and swelling are, by comparison, reasonably easy to assess with some degree of accuracy.

CLINICAL FINDINGS

Age Distribution

Table I reveals that the patients on the project were of similar age in both the G27202-treated and in the placebo groups.

TABLE I.—AGE

	Oxyphenbutazone		*Placebo*		*All patients*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Number of patients:	148		87		235	
Age: 15 - 24 years	67	45.3	47	54.1	114	48.5
25 - 34 "	55	37.2	26	29.9	81	34.5
35 - 44 "	15	10.1	5	5.7	20	8.5
45 and over	9	6.1	7	8.0	16	6.8
Not recorded	2	1.3	2	2.3	4	1.7

OPERATIVE PROCEDURES

In Table II, three-quarters of the patients were postpartum cases and had had an episiotomy performed. Approximately the same percentage of subjects fell into the group of cases clinically classified as having a moderate to severe operative procedure.

TABLE II.—OPERATIVE PROCEDURES

	Oxyphenbutazone		*Placebo*		*All patients*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Episiotomy	108	73.0	71	81.6	179	76.2
Cesarean section	19	12.8	4	4.6	23	9.8
Hysterectomy	12	8.1	7	8.0	19	8.1
Oophorectomy	3	2.0	3	3.4	6	2.6
Colporrhaphy (A and P repair)	4	2.7	1	1.1	5	2.1
Removal post. vagina	1	0.7	0	—	1	0.4
Removal mons and ant. abd. wall	1	0.7	0	—	1	0.4
Simple vulvectomy	0	—	1	1.1	1	0.4

DOSAGE AND DURATION OF TREATMENT

All but one patient received a loading dose of the drug, which was given preoperatively where practicable (Table III). Ninety-four per cent of the patients received the drug for a period of four to seven days.

TABLE III.—DOSAGE AND DURATION OF TREATMENT

	Oxyphenbutazone		*Pacebo*		*All patients*	
	No.	*%*	*No.*	*%*	*No.*	*%*
Dosage (per day):						
Initial:						
200 mg.	1	0.7	0	—	1	0.4
400 mg.	147	99.3	87	100.0	234	99.6
Maintenance:						
300 mg. in all cases						
Duration of treatment:						
1 - 3 days	3	2.0	0	—	3	1.3
4 - 5	0	—	2	2.3	2	0.9
6 - 7	117	79.0	64	73.6	181	77.0
8 - 14	22	14.9	20	23.0	42	17.9
Not recorded	6	4.1	1	1.1	7	3.0

RESPONSE OF THE PATIENT AND TIME INTERVAL

The response noted at the end of three days of therapy with either placebo or G27202 is shown in Table IV and was almost identical with that noted at the end of the full course of therapy.

TABLE IV.—RESPONSE OF THE PATIENT AND TIME INTERVAL

Response	*During first three days*		*At end of treatment*		
	No.	*%*	*No.*	*%*	
Oxyphenbutazone					
Complete	109	73.6	109	73.6	89.1
Marked	24	16.2	23	15.5	
Slight	10	6.8	15	10.1	
None	4	2.7	1	0.7	
Not recorded	1	0.7	0	—	
Total	148		148		
Placebo					
Complete	46	52.8	46	52.8	72.3
Marked	19	21.8	17	19.5	
Slight	14	16.1	18	20.7	
None	5	5.7	6	6.9	
Not recorded	3	3.4	0	—	
Total	87		87		

The difference between G27202 and placebo response rates is highly significant ($P < .01$). More than twice the number of patients (27.6%) showed slight or no response to placebo compared to therapy with G27202.

RESPONSE AND TYPE OF PROCEDURE

When the patients who had an episiotomy were considered alone (Table V), the difference between G27202 and placebo response was again highly significant. There was no statistical significance in the response to the two "treatments" in the major surgical cases, probably owing in part to the small

TABLE V.—RESPONSE VERSUS TYPE OF PROCEDURE

	Diagnosis					
	Episiotomy		*Other procedures*		*All patients*	
Response	*No.*	*%*	*No.*	*%*	*No.*	*%*
Oxyphenbutazone						
Complete	85	78.0	24	61.5	109	73.6
Marked	15	13.8	9	23.1	24	16.2
Slight	6	5.5	4	10.3	10	6.8
None	2	1.8	2	5.1	4	2.7
Not recorded	1	0.9			1	0.7
Total	109		39		148	
Placebo						
Complete	36	50.7	10	62.5	46	52.8
Marked	18	25.3	1	6.2	19	21.8
Slight	13	18.3	1	6.2	15	16.1
None	2	2.8	3	18.8	5	5.7
Not recorded	2	2.8	1	6.2	3	3.4
Total	71		16		87	

size of this series, and also because the drug had less effect.

RESPONSE VERSUS SEVERITY OF TISSUE INJURY

The response obtained is contrasted to the severity of the disease in Table VI. Those on G27202 therapy responded significantly better ($P < .01$) when the severity of the tissue damage was moderate to severe compared to those patients with slight tissue damage.

TABLE VI.—RESPONSE VS. SEVERITY OF TISSUE INJURY

	Severity of tissue injury					
	Mild		*Moderate*		*Severe*	
Response	*No.*	*%*	*No.*	*%*	*No.*	*%*
Oxyphenbutazone						
Complete	19	95.0	60	68.9	25	71.4
Marked	1	5.0	18	20.7	5	14.3
Slight	0	—	5	5.7	4	11.4
None	0	—	4	4.6	0	—
Not recorded					1	2.9
Total	20		87		35	
Placebo						
Complete	24	80.0	17	44.7	5	27.8
Marked	6	20.0	8	21.0	4	22.2
Slight	0	—	10	26.3	4	22.2
None	0	—	1	2.6	4	22.2
Not recorded			2	5.3	1	5.6
Total	30		38		18	

TYPE OF RESPONSE

Pain and swelling both responded significantly better to G27202 than to placebo ($P < .01$) (Table VII). Erythema was present in too few cases to allow a valid conclusion to be drawn.

TABLE VII.—TYPE OF RESPONSE

	Pain		*Swelling*		*Redness*	
Response	*No.*	*%*	*No.*	*%*	*No.*	*%*
Oxyphenbutazone						
Complete	111	75.0	106	74.6	3	33.3
Marked	18	12.2	23	16.2	4	44.4
Slight	19	12.8	12	8.5	2	22.2
None	0	—	1	0.7	0	—
Total	148		142		9	
Placebo						
Complete	42	48.3	45	52.3	1	14.3
Marked	19	21.8	21	24.4	1	14.3
Slight	22	25.3	16	18.6	4	57.1
None	4	4.6	4	4.6	1	14.3
Total	87		86		7	

TOXIC SYMPTOMATOLOGY

Side effects were noted in 16 of the 148 cases treated with G27202 (10.1%) (Table VIII). Only two of the 16 patients had symptoms which were thought to be due to the drug. In these cases the therapy was discontinued. One patient developed ileus while receiving the placebo. The administration of this agent was discontinued.

TABLE VIII.—SIDE EFFECTS ON EACH TREATMENT

	Oxyphenbutazone No.	*Placebo No.*
Total treated	148	87
Side effects:		
Gastritis	2	1
Nausea and vomiting	4	4†
Stomatitis	5	1
Diarrhea	1*	—
Ileus	1	1
Dizziness	1	—
Headache	1	1
Rash	1*	—

*Required discontinuance of drug.
†Required discontinuance of drug in one case.

DISCUSSION

When the results of this study were discussed with the ward nurses, after the punch cards had revealed the distribution of cases, it was recognized that a change had been apparent to the nursing staff during the study. The effect was observed in the reduction in the number of patients requesting specific analgesic drugs for relief of postoperative pain in the groups on G27202 therapy.

It is apparent that this drug is effective in the relief of pain and edema, but the maximum effect is obtained only after a loading dose and three days of therapy. This is in contrast to the accepted form of analgesic therapy, which is usually a single dose or one repeated every four to six hours as required for 24 hours, with the replacement of the agent by a milder analgesic for the next 24 hours at the same time intervals.

The necessity of a loading dose and the regular therapy for a minimum of three days will not be acceptable to many physicians and, further, the slow elimination of the drug may pose serious problems in the face of uncontrolled infection or the toxic or allergic response to the drug by the patient.

Five patients on treatment with G27202 have developed severe postoperative infection. None of these was given prophylactic antibiotics, either preoperatively or postoperatively.

Three of the patients developed moderately severe but localized wound abscesses which were controlled by drainage and the administration of an appropriate antibiotic. One patient developed a moderately severe pelvic abscess, after repair of a sacro-pubic hernia, which responded to the same therapy.

One patient, after total hysterectomy, was asymptomatic and afebrile until the fourth day, when a severe subcutaneous infection developed, which tracked almost around the circumference of the abdominal wall. Multiple incisions and treatment with a high dosage of specific antibiotics were necessary before the mixed infection (due to hemolytic and gas-forming anaerobic streptococci) was brought under control.

Most of the infections which have been encountered in the patients on G27202 therapy have been

unaccompanied by high temperatures, and no patient has complained of severe localizing pain. The drainage wounds are slow to granulate and close.

One further observation is of importance. In this series of 235 patients there were 11 who developed superficial thrombophlebitis involving one or both lower extremities, one who developed a superficial thrombophlebitis from an intravenous needle puncture in the antecubital vein, four with deep phlebitis involving the femoral vein, and one with migratory superficial thrombophlebitis which was associated with abdominal carcinomatosis of ovarian origin.

It was first noted that a few patients who developed superficial thrombophlebitis while on the study, were symptom-free and were found to have only a cord-like, fibrous reaction in the involved veins of the leg. The next six patients who developed superficial thrombophlebitis were placed on G27202 empirically. Pain and tenderness were relieved, in most cases, within 36 hours and the palpable masses usually disappeared within four weeks. This finding has been noted by others.[8]

Because of one or other contraindications to anticoagulant therapy, four patients with deep phlebitis were placed on G27202. Again, the pain and tenderness were relieved within 36 hours and the edema of the lower limb gradually subsided over four to five days. Thus far, no patient with deep phlebitis has developed a chronically swollen leg and there is no sign of a postphlebitic syndrome in any of the patients.

The patient with abdominal carcinomatosis of ovarian origin who developed a migratory superficial thrombophlebitis postoperatively was placed on G27202 therapy for nine weeks until her death. The drug did not prevent the occurrence of the phlebitis but allowed the patient to live out her remaining days, relatively free of pain which usually occurs with the multiple, inflamed and obstructed venous channels.

To date, no alteration in the clotting mechanism has been noted in patients receiving G27202. Routine hemoglobin, white blood cell counts and sedimentation rates reveal no change from normal. Several patients have exhibited a lowered prothrombin consumption, but this is regarded by hematological consultants as being of questionable significance. We have no explanation of the mechanism of action of the drug on the blood clot in the thrombosed vessels.

SUMMARY

Oxyphenbutazone, a metabolite of phenylbutazone, was assessed for anti-inflammatory properties in a double-blind study at the Royal Victoria Maternity Hospital in Montreal.

The drug was well tolerated and no serious side effects were noted. The discontinuance of therapy was necessary in only two patients.

The drug has a maximum effect after three days of therapy; the difference in response of patients treated with oxyphenbutazone compared to that of subjects given a placebo was statistically significant in those with episiotomies and in those with moderate to severe surgical trauma.

Pain and swelling were markedly reduced in those patients on oxyphenbutazone therapy.

The anti-inflammatory activity of the drug is of therapeutic value, in both superficial and deep phlebitis, relieving pain within 36 hours and edema within 72 hours. No postphlebitic swelling or pain has been noted in four patients with deep phlebitis who have been followed over nine months.

The anti-inflammatory action of the drug is thought to interfere with the localization of infection. Several of our patients exhibited little temperature fluctuation or local pain in the presence of serious postoperative infections.

Further investigation of this compound is being undertaken.

We are very much indebted to Miss Elizabeth Hughes, R.N,. for her invaluable assistance in conducting this double-blind study.

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PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The national importance of a careful consideration of infant mortality has been brought to the notice of sanitarians and the public during the past few years, and we have, fortunately, much valuable information upon the subject, chiefly derived from the older and more densely populated countries where all those varying conditions of environment consequent upon density, occupation, and poverty, have most important bearings upon the lives of the infants; conditions, as we often pride ourselves, which either do not exist in this country, or, if they do exist, are so slight as not to be worthy of consideration.

The registrar general of England and Wales in a study of this subject has made many interesting comparisons in his annual report; and Dr. T. H. C. Stevenson, in the seventy-first annual report (1903), states that, "during the greater part of twenty-eight years (1881-1908) there has been no fall in the rate of infantile mortality in England and Wales." In that country, from 1881-1899 the rate was slightly on the ascendant, but since 1899 the rise has been compensated for by a considerable fall—a fall due possibly to the quickening of the public conscience upon the subject, —a feature also noticeable in the returns of Prussia, Norway and Denmark.—C. A. Hodgetts, Infantile Mortality in Canada, *Canad. M. A. J.*, 1: 720, 1911.

DIABETES MELLITUS: A STUDY OF THE PRACTICABILITY OF LIFE INSURANCE

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IN 1940 THE Manufacturers Life Insurance Company first started offering life insurance to known diabetics. Since that time, in the series of policies put in force on known diabetics there have been 126 deaths involving 174 policies for a total death benefit of $1,850,091. There are now over 1300 such policies in force for over $17,000,000. The material presented in this paper concerns (1) the cause of death for all those who have died in the Manufacturers Life diabetic group from 1940 to 1960; (2) an examination of the comparative mortality experience or rate of dying of our insured diabetic group during 1950 to 1960, compared with the mortality experience of a normal, healthy group of insured policyholders.

The criteria for classifying these people as diabetics are: (a) admission of the diagnosis of diabetes by the applicant; or (b) a report from the attending physician that the individual concerned was considered to have diabetes mellitus; or (c) a blood glucose tolerance test with a two-hour level over 130 mg. per 100 c.c. of blood.

In many of the cases blood sugar levels were not available and the diagnosis rested entirely upon the report of the attending physician.

1. *Cause of Death in Insured Diabetics, 1940-1960*

One hundred and twenty-six insured diabetics died during the period 1940-1960. Table I shows their age at the onset of the diabetes. Slightly over half of the group had this onset between the ages of 30 and 49 years.

TABLE I.—AGE AT ONSET OF DIABETES IN INSURED PERSONS WHO DIED IN THE PERIOD 1940 - 1960

Age at onset	*Number*
10 - 19	16
20 - 29	21
30 - 39	31
40 - 49	36
50 - 59	20
60 +	2
	126

The duration of diabetes at the time of death is shown in Table II. Over one-half of the patients died after having had diabetes for 11 to 20 years.

The greatest cause of death was cardiovascular-renal involvement. This is shown in Table III, where it is compared with the total company experience on insured lives. Although the figures are too small to be significant, suicide is responsible for an increased proportion of deaths in the diabetic series, and cancer and accidents are less common in the diabetic series. Of 126 deaths, three were attributed to diabetic coma and one to insulin shock.

TABLE II.—DURATION OF DIABETES AT TIME OF DEATH: INSURED LIVES, 1940 - 1960

Duration of diabetes	*Number*
1 - 5 years	10
6 - 10 "	20
11 - 15 "	23
16 - 20 "	43
21 - 25 "	16
26 - 30 "	6
31 - 35 "	7
36 - 40 "	1
	126

Of 77 heart disease deaths, 67 were reported as due to coronary artery disease and 10 as "cardiac deaths".

There were 11 "vascular deaths", 10 due to cerebral hemorrhage and one to mesenteric thrombosis.

The figures for the total company experience are based on 9829 deaths which occurred during 1952, 1954, 1956 and 1958.

TABLE III.—CAUSE OF DEATH

	Diabetic persons %	*Control group* %
Cardiac	61.0	42.5
Vascular	8.7	10.5
Renal	8.8	1.0
	78.5	54.0
Cancer	7.9	19.0
Suicide	4.8	2.0
Accident	2.4	8.5
Diabetic coma	2.4	—
Diabetes	—	2.0
Acute respiratory	1.6	2.3
Insulin shock	0.8	—
Infection	0.8	—
Portal cirrhosis	0.8	—
Miscellaneous	—	12.3
	100%	100%

Insured diabetics, 126 deaths, Manufacturers Life Insurance Company, 1940 - 1960.
Control 9829 deaths—total Company deaths, 1952, 1954, 1956 and 1958.

If we assume, as seems likely from the rest of this study, that the rate of dying of the diabetics insured in this group is twice that of the total company experience, the material can be presented to show the "extra deaths" (Table IV). This is a comparison based on crude cause of death and comparing 200 diabetic deaths with 100 of the total company experience as a control.

While the material in Table IV is a comparison involving crude, not age-specific, death rates, it suggests that the extra mortality among the insured diabetics is concentrated in the cardiovascular-

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TABLE IV.—HYPOTHETICAL EXTRA DEATHS IN INSURED DIABETICS

Cause of death	*Diabetic deaths*	*"Control"*	*Difference*
Cardiovascular	139.4	53.0	+86.4
Nephritis	17.6	1.0	+16.6
Suicide	9.6	2.0	+ 7.6
Diabetic coma	4.8	0	+ 4.8
Acute respiratory	3.2	2.3	+ 0.9
Cancer	15.8	19.0	− 3.2
Accident	4.8	8.5	− 3.7
Others	4.8	14.2	− 9.4
	200.0	100.0	+100.0

renal group, augmented slightly by suicide and diabetic coma. Miscellaneous causes, accidents, and cancer seem to contribute less than their expected share of deaths in the diabetic series.

from the study that the younger diabetics showed a higher percentage mortality.

It was customary to request an electrocardiogram on applicants for policies over $10,000 and on those over age 40. The first line in Table V, "No other impairments, no electrocardiogram", with a mortality ratio of 183% by amount and 192% by policy, probably represents the younger applicants and the policies of smaller amounts. This may explain why the ratios in line 1 are higher than those in line 2, "No other impairments, normal electrocardiogram", which shows 144% by amount and 157% by policy. The length of exposure in both of these groups is sufficiently large to make the figures reasonably accurate.

The remaining lines in Table V show the experience when other impairments are present in

TABLE V.—EXPERIENCE ON INSURED DIABETIC PERSONS DURING 1950 - 1960

	By amount			*By policies*		
	Exposure ($ years in millions)	*Claims (in thousands of $)*	*Ratio of actual to expected*	*Ratio of actual to expected*	*Claims by number of policies*	*Exposure (policy years)*
No other impairments. No EKG	22.0	191	183%	192%	36	4133
No other impairments. EKG normal	65.7	732	144%	157%	45	4435
Overweight ± other impairments	5.2	50	*129%	*178%	4	345
Blood pressure elevation ± other impairments	4.0	77	234%	529%	9	350
EKG abnormal, no other impairments	5.2	155	509%	769%	12	261
Albuminuria	0.4	18	*2040%	*2730%	3	66
Miscellaneous other impairments	15.2	131	143%	423%	14	798
Total	117.7	$1354	168%	215%	123	10,388

*Insignificant amount of exposure.

2. *The Comparative Mortality Experience from 1950 to 1960*

The comparative mortality ratios are determined by examining the deaths which occurred in the group studied, compared to the deaths expected in a similar group of normal lives, the ratios being expressed as percentages. In this instance the normal mortality is taken from the 1946-1949 Select Basic Table which is compiled from an intercompany study of the death rates experienced during 1946-1949 on applicants for insurance who were medically examined and issued standard insurance. As the death rates between 1946 and 1949 were slightly higher than in the 1950's, the mortality ratios shown in this paper are slightly less than they would otherwise be.

Table V shows that the total experience for the insured diabetic persons during 1950-1960 is 168% by amount and 215% by policy. The amount paid in death claims was $1,354,000. This was covered by 123 policies on 94 persons.

The smaller policies showed a disproportionate share of the deaths, possibly owing to less careful selection of persons at the time of issue. Other explanations might be the chance issue of multiple policies to those who happened to die, as well as the usual tendency for the monetary value of policies on younger lives to be small. It is apparent addition to diabetes. In each case the figures are small and the possibility of chance fluctuation is great.

Overweight was not associated with an increased death ratio, being 129% by amount and 178% by policy. This may be due to chance, since the group was very small.

Diabetes plus slightly increased blood pressure, with and without other impairments, gave high ratios of 234% by amount and 529% by policy.

Diabetes plus electrocardiographic abnormalities gave a higher ratio of 509% by amount and 769% by policy. All the electrocardiograms coded as "not entirely normal" were reviewed and showed minor variations which, clinically, would be considered normal or possibly borderline. The 12 policies that were terminated by death were held by five persons, two having four policies each and one having two policies. The abnormalities in these electrocardiograms were:

1. Extrasystoles. One person had four policies and died of cerebral hemorrhage four years after issue. One person with one policy died of arteriosclerotic heart disease 1½ years after the date of issue.

2. Low T-V 5 & 6, flat T-AVL. One person with four policies died of coronary thrombosis 2½ years after issue.

TABLE VI.—DURATION OF DIABETES AT TIME INSURANCE ISSUED

	By amount		By policy	
	Claims (in thousands of $)	*Ratio of actual to expected*	*Ratio of actual to expected*	*Number of policies terminated by death*
0 to 5 years	237	81%	136%	29
6 to 10 "	213	159%	213%	24
11 to 20 "	453	288%	217%	26
21 to 30 "	20	75%*	77%*	2

*Insignificant amount of exposure.

3. QRS of 0.11 second: Right bundle branch block configuration. One person with two policies died of coronary occlusion 9 years after issue.

4. Low T-1. One person with one policy died of myocardial infarction 4½ years after issue.

These figures are obviously too small to be of much value, although, statistically, they have some significance.

TABLE VII.—INSULIN DOSAGE

	By amount		By policy	
	Claims (in thousands of $)	*Ratio of actual to expected*	*Ratio of actual to expected*	*Number of policies terminated by death*
No insulin.....	286	103%	125%	22
1 - 24 units of insulin daily	91	104%	163%	13
25 - 49 units of insulin daily	375	219%	218%	31
50 or more units of insulin daily	171	226%	194%	15

Albuminuria associated with diabetes gave very high ratios, over 2000% by amount and by policy, but there were only three deaths in insured persons. Applicants with diabetes and albuminuria were usually refused insurance.

TABLE VIII.—URINALYSIS

	By amount		By policy	
	Claims (in thousands of $)	*Ratio of actual to expected*	*Ratio of actual to expected*	*Number of policies terminated by death*
Sugar in urine at time of application				
0 to 0.1%	437	117%	145%	42
0.15 to 0.3%	81	130%	193%	9
over 0.3%	405	232%	218%	30

The experience represented by the first two lines in Table V was studied further. These results are shown in Tables VI to IX. These diabetics, with no other impairments and with normal electrocardiogram if one was taken, were studied according to duration of diabetes, insulin dosage, amount of sugar in urine, frequency of blood sugar test, average blood glucose level, and frequency of visits to the doctor. Inquiry was also made concerning insulin reactions, diabetic coma and diabetic retinitis.

TABLE IX.—FREQUENCY OF BLOOD SUGAR DETERMINATION

	By amount		By policy	
	Claims (in thousands of $)	*Ratio of actual to expected*	*Ratio of actual to expected*	*Number of policies terminated by death*
Blood sugar yearly or oftener...	631	137%	159%	54
Blood sugar less than yearly..	267	244%	211%	20

It should be kept in mind that these measurements of the severity and control of the diabetes are only made available to the company at the time that the diabetic takes out his life insurance policy. It is not possible to determine subsequent changes in any of the measurements after the policy is issued.

Table VI, dealing with duration of diabetes, shows that the mortality ratios increase as the duration of diabetes increases. There were very few applicants who had had diabetes for over 20 years at the time of applying for a policy and therefore the figures for that group are not significant.

Table VII, concerning insulin dosage, shows higher mortality ratios as the amount of insulin required for treatment increases. Applicants for insurance who were taking more than 50 units of insulin per day were considered severe diabetics and were offered insurance only if other attributes were very favourable. Practically none of the insured were on oral hypoglycemic therapy.

Table VIII, concerning urinalysis, shows that the mortality ratio increased with the amount of sugar in the specimen examined at the time of application.

Table IX, which deals with blood sugar, suggests that the frequency of determining blood sugar level was important. In some persons in this group the blood sugar frequency was unknown and these are omitted from Table IX.

There were not enough data on the presence or frequency of insulin reactions to be useful.

Very few diabetic persons who had a history of diabetic coma were offered insurance. There were two persons holding policies in this group who made claims for $12,500, 650% by amount and 1170% by policies. This sample is too small for the figures to be meaningful.

The presence of retinitis was cause for refusal of insurance. Accordingly, there is practically no experience available in this series regarding mortality of diabetics with retinitis.

In the total series, as shown in Table X, diabetics insured at ages 20 to 29 years, who had diabetes for 11 or more years at the time they were insured, showed a high mortality ratio both by policy and by amount. Also, after age 50, those who had been diabetic for 11 or more years at the time of

TABLE X.—DURATION OF DIABETES AT THE TIME OF POLICY ISSUE AND PERSON'S AGE AT ISSUE

		By amount			*By policy*		
Duration of diabetes	*Age at issue*	*Exposure ($ years in millions)*	*Claims (in thousands of $)*	*Ratio of actual to expected*	*Ratio of actual to expected*	*Number of policies terminated by death*	*Exposure in policy years*
0 - 10 years at issue	15 - 29	3.7	5	118%	130%	1	686
	30 - 39	19.6	88	165%	220%	13	2188
	40 - 49	33.6	319	151%	208%	36	2654
	50 - 59	15.4	283	184%	280%	26	888
	60 and over	6.6	91	76%	89%	5	291
	Total	78.9	786	145%	207%	81	6707
11 + years at issue	20 - 29	2.1	46	1830%	1210%	7	461
	30 - 39	12.2	40	107%	165%	8	1669
	40 - 49	11.2	76	107%	135%	10	1122
	50 - 59	10.8	221	254%	257%	10	368
	60 and over	2.5	185	277%	543%	7	61
	Total	38.8	568	214%	233%	42	3681

application for insurance showed comparatively high mortality ratios.

Three-quarters of the persons on whom this study was based were residents of the United States; most of the remainder were residents of Canada and a small number were from other countries where the company has branches.

Ninety-eight per cent of the experience was on males, 2% on females.

TABLE XI.—50% STATISTICAL CONFIDENCE LIMITS

	Observed morality ratio		
Actual deaths	*150%*	*250%*	*350%*
5	102% - 222%	170% - 370%	238% - 518%
10	116% - 195%	193% - 325%	270% - 455%
25	129% - 176%	215% - 293%	301% - 410%

The comparative mortality ratios of diabetic lives to those of a group of standard lives gives an indication of the true level of mortality. The ratios, however, are subject to the statistical variation of chance fluctuation, particularly when the number of lives and the number of deaths in that group are small. Table XI is provided to show the range in which the true mortality ratio falls by a 50% chance. For example, in a group with 10 deaths and a mortality ratio of 250%, using the table, there is a 50% chance that the true mortality ratio for a very large group of similar lives is within the range 193 to 325%.

The figures presented here concern diabetics who were carefully selected before life insurance was issued and do not apply to diabetes in general. Many persons with diabetes who applied for life insurance were refused and others did not accept the insurance.

SUMMARY

The mortality experience among carefully selected insured diabetic persons is presented.

Insured diabetics show an increased mortality from cardiovascular-renal disease.

Those who have diabetes from early in life and those who have had diabetes for over 10 years at the time of being issued a policy show comparatively high mortality ratios.

The duration of the diabetes, the amount of insulin used, the amount of sugar in the urine, and the frequency of determining blood sugars seem to be important in anticipating mortality ratios.

With the co-operation of the physician, including the completion of life insurance questionnaires dealing with the insured person, and the observance of the doctor's instructions by the "patient", life insurance can be offered to selected diabetics with allowance for a moderate extra mortality.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

The following figures (Table I) may be taken as representing the reckless and wanton destruction of infant life which prevails in different countries, the figures being for the year 1908, with the exception of France, which is for 1907. A comparison of some of the British colonies is shown in Table II, the figures for the provinces of Ontario and Quebec being included.

TABLE I.—INFANTILE MORTALITY
DEATHS OF CHILDREN UNDER 1 YEAR TO 1,000 BIRTHS

1908—Foreign Countries

Chili	320	Netherlands	125
Hungary	199	Denmark	123
Prussia	173	Scotland	121
Bulgaria	170	England and Wales	120
Servia	158	Switzerland	108
Japan	157	Ireland	92
Italy	153	Sweden	85
Belgium	147	Norway	76
France (1907)	135		

TABLE II.—INFANTILE MORTALITY
DEATHS OF CHILDREN UNDER 1 YEAR TO 1,000 BIRTHS

1908—British Colonies

Ceylon	183	Western Australia	85
Jamaica	175	New South Wales	76
Quebec (1906)	128	Tasmania	75
Ontario	124	Queensland	70
Canada (1901)	120	S. Australia	70
Victoria	86	New Zealand	68

SPECIAL ARTICLE

MEDICINE IN A CHANGING WORLD*

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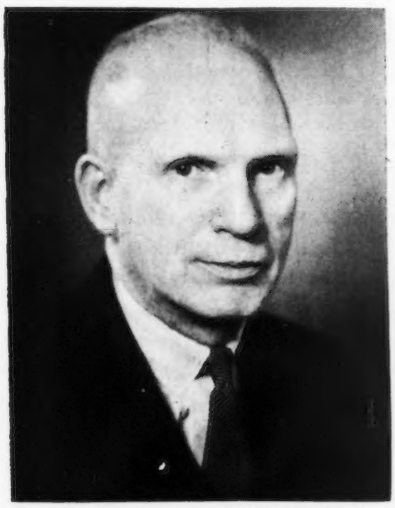

Stillings, Calgary

Dr. R. MacGregor Parsons

WHEN addressing the Royal College of Physicians in 1944, Winston Churchill said: "The longer you can look back the further you can look forward."

While preparing this address I have read with great interest Dr. Ernest MacDermot's history of the Canadian Medical Association. It makes absorbing reading and brings to light many interesting phases in the development of Canadian medicine. After World War I the organization would surely have disbanded, but for Clarence Routley, our Secretary for many years, and some of his sturdy supporters. Our secretariat continues to demonstrate this forceful leadership.

The C.M.A. was organized in 1867 in Quebec City. The objectives, which can be stated briefly, were to promote health and prevent disease; to improve medical services and to maintain the honour and integrity of the medical profession. The actual objects, as adopted, provide interesting reading almost a century later and show that our forebears had vision and imagination. They were:

- To give frequent, united and decided expression of the medical opinion of the country.
- To advance medical knowledge.
- To elevate the standards of medical education.
- To direct and control public opinion in regard to the duties and responsibilities of medical men.
- To excite emulation as well as harmony in the profession.
- To facilitate and foster friendly intercourse among its members.

I think that all will agree that these objectives are a challenge to the medical profession today—as they were in 1867.

Of all the stresses to which man is exposed, one is constant: the threat of illness. When beset by sickness, people turn to their doctor with faith and respect. Many forces are threatening this bond which has always existed between patient and doctor. Although the average physician today has the complete respect and confidence of his individual patient, the average layman is uneasy about the profession as a whole. Perhaps we are at a most important crossroad in our relationship with the public. I would like to explore the charge that this relationship is becoming impersonal and that the service we render has deteriorated.

It appears that recent advances in the science and economics of medicine have far outstripped those in the art. These advances are so specific and dramatic that they take away attention from the patient as a whole. Years ago Dr. W. J. Mayo said that success in medicine depends 90 to 95% on personality and 5 to 10% on knowledge and ability. Today we know that these figures have changed significantly.

In the past 30 years there has been a great change in the type of practice, and the patient has been seen more and more in the office and in the hospital. In years past, if the patient came to the hospital for anything but surgery he felt that his chances of recovery were not good. It was difficult to persuade the sick to come to hospital, but now it is hard to persuade or convince them that under some circumstances they are better off at home.

Obstetrics was practised mainly in the home and there was a much closer relationship between the doctor and the patient and his family. Although the patient often is not as happy in the more impersonal surroundings of the hospital, the professional care possible in the office and hospital cannot be duplicated in the home. Forty years ago, to treat pneumonia the general practitioner had aspirin, mustard plasters and fluids. Short of drugs and other gifts of science, the doctor had to give to the patient of himself. He practised the art of medicine. Many hours were spent with the patient and his family because he had so little else to give them. Compare this situation with that of today when he may see a patient with severe pneumonia one day, prescribe an antibiotic and find the infection resolving in 24 hours. The doctor has so much to offer the patient scientifically that there is not the same requirement for the art in his daily practice. Unfortunately, this advance in technology does little either to maintain the dignity of the

*The Presidential Address delivered to the Divisions of the Canadian Medical Association, 1960-61.

patient as a person or to enhance the public image of the physician.

Another feature of modern medicine is the increase in physicians in specialty practice. The Greek historian Herodotus, writing in the 5th century B.C., said, "The art of medicine of the doctors of Egypt is distributed thus: each physician is a physician of one disease and no more; the whole country is full of physicians, for some profess themselves of the eyes, others of the head, others of the teeth, others of the affections of the stomach and others of more obscure ailments."

Early in our own medical history, at the C.M.A. Annual Meeting in 1881, the following resolution was brought in: "Whereas specialism obtains to a certain extent in the Dominion and has developed to very large proportions in the neighbouring Republic, it is for the most part an outgrowth of superficial professional education and want of success as practitioners of medicine and surgery. Therefore be it resolved that: It is the opinion of this society that specialism should be discountenanced by members of the society and that specialists except in rare cases where long experience, extended study, and peculiar aptitude have placed a man in a special position toward his brethren—should be treated and looked upon as irregular practitioners." The motion was *not* passed.

The cycle is almost complete and more than a third of our profession are in this "special position" toward their brethren carrying on the practice of a specialty.

At least 50% of Canadians have some form of sickness insurance, and more and more people seek medical care. This is in part due to the campaign carried on by the press, insurance companies and health organizations which urges the public to see their doctor before it is too late, and they have taken this advice seriously. Medical information and much pseudomedical information is widely disseminated through many channels—books, magazine articles, radio, television and medico-lay societies. The patient often makes his own diagnosis and expects, and frequently demands, certain investigations and treatments based on this home-made diagnosis. Under these circumstances the physician may be obliged to justify a diagnosis and treatment, arrived at by scientific means, and must do so against the patient's opposition.

Our civilization has produced great technical achievements and an increasing mechanization of life—rural living giving way to large urban concentrations. There seems to be a general dehumanization of everything. *Things* mean more than *people* and the *individual* counts for *less* and *less*. This universal depersonalization is bound to have some repercussions in medicine. There is a change in moral values, as portrayed in Oliver Goldsmith's immortal lines:

> When lovely woman stoops to folly
> And finds too late that men betray,
> What charm can sooth her melancholy
> What art can wash her guilt away.

In 1780 she had only one recourse:

> The only art her guilt to cover
> To hide her shame from every eye
> To give repentance to her lover
> And wring his bosom—is to die.

In the early 20th century, T. S. Eliot gave her a further choice:

> When lovely woman stoops to folly and
> Paces about her room again, alone
> She smooths her hair with automatic hand
> And puts a record on the gramophone.

In 1960, apart from norethynodrel, she has a wide range of tranquillizers from which she can choose.

What are the specific complaints of those who have available medical care? According to a recent survey in 'Life' magazine, the complaints were that doctors could not be reached in emergencies; did not spend enough time with their patients; charged too much; and made mistakes in diagnosis and treatment. A distinguished surgeon was quoted as saying that half his practice consisted of correcting the bad results of surgery done by inadequately trained doctors. At all levels there is less time for the patient. There are a greater number of diagnostic methods to be used upon him, especially in hospitals. The patient gets the impression that everything is being done to speed his recovery; but he is anxious because there is much that he does not understand. When a doctor does visit, it seems to him at times that the newspaper headlines of the paper on his bed are of more interest than what he has to say. A few words of comfort and understanding can often work wonders. Richard Asher asks if a specialist should show special indifference and ignorance of all other branches of medicine. Should he not rather be a jack of all trades and a master of one? Can a surgeon not prescribe a simple obesity diet rather than refer the patient to an endocrine clinic?

Terms that are familiar and in daily use by a medical man are often confusing to the patient. The doctor often uses neither the language of science nor that of art but something in between: medical slang. He places a patient on penicillin, or sits on an acute belly for 24 hours. This can be most confusing to the patient. Most patients do not understand what is meant by herpes zoster. When we say shingles, we still have patients whose grandmothers have told them that if they meet in the middle, it is sure death. We put adhesive on hairy legs and do not know the very high cost of some drugs. We are accused of over-investigation and over-treatment. If a patient is dying from secondary cancer we try to find the primary site. Our explanation for this is that "hope springs eternal" and the discovery of a cure may come about suddenly.

What can we as a profession do about all this? In the first place, as doctors, I feel we should worry less about the "corporate image" of medicine and more about our individual relationships. It has been said that the first requisite in caring for the patient is caring about the patient. There is still no test for measuring the intangible qualities of a man that fit him for the service of humanity in medicine. Committees selecting future medical students have a serious duty and our medical schools are attempting to assess medical students on their moral fibre as well as on their academic marks. They are attempting to accept those who care about people, those who like their fellow men and are concerned about them. In some places the medical student comes in frequent contact with patients throughout his academic course and learns to relate everything to the person. MacMurray has said: "Just as a teacher who teaches his subject and not his pupils is a bad teacher, so a doctor who sets out to heal diseases instead of healing people will not be a good doctor. The patient as a person requiring help is the focus of all problems in medicine. There must be something the matter with a patient who comes to the doctor when there is nothing the matter with him. The anxiety must have a cause and is itself a disease." Fear is the primary emotion of the sick person, and he needs explanation, encouragement and reassurance.

In the second place, as an Association I think we are probably at the most important era in the history of medicine in Canada. Through this journal, our members are familiar with the events that led up to the request of this Association and the appointment of a Royal Commission to explore the health resources and needs in Canada, which resulted from it.

This Committee will collaborate closely with the secretariat concerning all dealings of the Canadian Medical Association with the Royal Commission. There will be many briefs and the attitude of our profession will be exposed in our own eyes and in the public mind. Our attitude should be that of a single body and not of many factions and, as C.M.A. President, I make a plea for unity at this time. The many bodies of Canadian medicine are largely the lusty children of and Divisions within the Canadian Medical Association, but our attitudes in these vital matters should be not divided but one. There will be many facets of thinking; but one main attitude. Medicine is a profession and as such is interested in service to mankind—our critics to the contrary. This is the time for medicine to speak with a common voice with respect to its devotion to service.

Actually, the approach of the doctor to life should be the measure of him. What is this approach? Any doctor who is worth his salt is interested in saving human lives and preserving health. He is interested in equipping himself as best he can to save human lives. This involves medical education and this is the reason that the Canadian Medical Association was formed. He is interested in medical research. As the Honourable Waldo Monteith, Canada's Minister of National Health and Welfare, said in a recent speech, "Medical research holds an important key to the future welfare of all Canadians."

The physician has no other motive, although he is often suspected of others. His objective is to give the people the best possible chance to live in good health. His philosophy is concerned with how best to equip himself to save human lives. We convince our fellow citizens of this only by performance. When we describe or set down on paper our plans for medical care, in whole or in part, they must be such that they will stand any analysis, investigation or debate—that they are demonstrably in the best interests of the people of Canada. When we do that, the problem of economics in medical care will have been solved.

Finally, after having practised medicine for nearly 30 years in one community and having visited most of the Divisions, I believe that my medical colleagues, measured by any yardstick and compared with other professional people or any other citizens in the community, have stood the test of time. I am sure that each Canadian doctor feels the same way about his colleagues. For the most part the Hippocratic Oath has been an important factor in guiding our lives, and many of the accusations aimed at the profession today result from changes in trends and methods of treatment rather than from any change in basic character of the individual physician. The physician still assumes responsibility in all walks of life and generously passes on to the new generation of doctors what he has learned from his predecessors.

I do hope that we can make science our slave rather than our master and plead that all of us reexamine ourselves in relation to our patients and determine if we have kept the same interest in the people encountered in our day-to-day work as we have in its scientific aspect.

PAGES OUT OF THE PAST: FROM THE JOURNAL OF FIFTY YEARS AGO

PRINCIPAL CAUSES OF DEATHS OF INFANTS, CANADA, 1901

Congenital debility, 6,388.

Diarrhoea, including cholera morbus, dysentery, epidemic dysentery, 5,477.

Diseases of the nervous system (simple meningitis, 1,277; convulsions, 1,101), 2,378.

Diseases of the respiratory system (pneumonia, 1,001; acute bronchitis, 584; broncho-pneumonia, 359; congestion and apoplexy of the lungs, 312), 2,256.

Acute infectious diseases (whooping cough, 578; diphtheria, 677; influenza, 460; measles, 334; scarlet fever, 159), 2,308.

Tuberculosis of all forms, 564.

Inanition (want of breast milk), 323.

—C. A. Hodgetts, Infantile Mortality in Canada, *Canad. M. A. J.*, 1: 720, 1911.

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GENERAL PRACTICE

LET'S FACE THE FACTS*

F. MURRAY FRASER, M.D., *Halifax, N.S.*

IN THE latter half of the 17th century, a happy little Dutch naturalist, Anton Leuwenhoek, squinted through the finest lens he had yet ground for his home-made microscope and said, "I have no other purpose than to place truth before my eyes, so far as it is in my power to embrace it." Let us put our medical lives under Leuwenhoek's lens, bring it gently into focus, and face the facts we see there.

Let's face the fact that governments, federal and provincial, must accept some responsibility for the provision of medical services to certain groups of our citizens. As it is the duty of a father to give his children protection against starvation, poor housing, ill health and the other hazards of life until they can assume these responsibilities for themselves, so it must be the duty of those we elect to govern us to provide, among other things, the finest medical care to those unable to do so for themselves.

This responsibility of government has grown out of the advances we ourselves have made in medicine. Whether we like it or not, it is to our glory. The two-dollar house call which often gave our patient the best professional advice 50 years ago may now, with specialist consultations and laboratory studies, end in a cost of one hundred times two dollars. Our patient is getting better care; he must pay for it, or somebody else must. So let's stop talking of the "threat" to medicine under the awakened interest of government in this problem and wholeheartedly co-operate to produce a system good for both the recipient and the donor, thereby removing the threat, of misguided though no doubt well-meaning individuals, to impose upon the nation a compulsory, comprehensive medical service with all its attendant evils. By our voluntary co-operation, we shall not only help maintain the dignity, the idealism and the freedom of medical practice, but can make a constructive contribution to national welfare in a field the physician knows better than any government agency.

Let's face the fact that the "doctor-patient" relationship, of which we speak so glibly, is on the way to extinction. Let's stop talking about its preservation. It dates us! The advent of prepaid medical care plans, of government-sponsored health care, of labour-inspired medical clinics and of provincial hospitalization plans has all but* destroyed that traditional war-cry of medicine. We in our development of "group" practice have hastened its destruction. The patient of today, on the plea that even his doctor needs "some time off", is taught to accept "the man on duty". Was it not a former Governor-General of this country who commented that his illness brought forth not a doctor but a "team of doctors"? The doctor-patient relationship will last only so long as the middle-aged doctor and his old patient survive and can reminisce together about the "good old days". Then it will be relegated—sadly, perhaps—to the limbo of the horse and buggy.

Let's face the fact that this College of General Practice was organized to provide for and encourage the continuing education of the general practitioner; that discussions of, and decisions on, politico-economic factors affecting the practitioner belong with our Sections of General Practice in the Divisions of the Canadian Medical Association, which was founded and developed primarily for this purpose. Economic decisions require the full support of all medical groups if these ends are to be accomplished. If we do not accept this, we shall become afflicted with all the dissensions and wranglings which characterize any organization composed of rugged individualists, and our educational aims will be lost.

Let's face the fact that it's time that Canada had a school of postgraduate medical studies and that the College of General Practice must be prepared to advise and support such a move. Every medical school in the country is attempting to bolster its reputation and enhance its prestige by provision of facilities for postgraduate and research work, in many instances to the detriment of undergraduate education. Is it their function to turn out specialists or to produce high-grade general practitioners for our largely rural population? Let's make up our minds on this point. If the medical schools were to restrict their teaching to the fundamental training of good family doctors, the course could be reduced by one year, if not two years, and the cost proportionately. This would make a career in general medicine available to a large group of excellent students who, at present, because of time or financial limitations, must enter other vocations. We are only beginning the age of specialization—a development which, in the light of the tremendous advances in medicine and surgery, past, present and future, is as natural as the growth of a child. Nowhere in the world is the quality of specialist education higher than in our own medical schools, but let there be a re-assessment of the areas of responsibility for this training.

Let's face the fact that those of us who take the fresh medical graduate as an assistant, introduce him into a ready-made practice (a practice

*The Presidential Address to the Annual Scientific Assembly of the College of General Practice of Canada, Vancouver, B.C., March 29, 1961.

which may have taken years to build), provide him with full clerical and nursing assistance, and give him regular time off and holidays are undermining the growth of responsibility, the maturation of the sense of accomplishment – and sacrifice – of that young man. It would be far better to send him into the rural areas of our vast country to *work* for a year; to share the hardships, the frugality, the worry and fatigue of many of our rural colleagues; to develop the self-confidence and humility that comes with the realization of "aloneness" in the battles of life and death, pain and suffering which will confront him. Having thus introduced him to the wonder and mysteries of general practice and the glorious sense of achievement which can ensue, let us provide the facilities for his continuing and higher education by the provision of short-term courses leading to certification in the field of his choice. Without his assistance we might have to work the harder or, bringing him in as an experienced, tested man, pay him more. But by so doing would we not be building a more rugged, wiser profession, with a mature understanding, tolerance and humility?

Let's face the fact that in the eyes of our sickly patients we may be demigods; in the eyes of the collective public we seem to be a group of monopolistic money-grubbers, bloated with self-importance, intolerant of intrusion into our private domain and martyred in pseudo-sacrificial devotion to our indigent brethren.

Let's face the fact that too many of us besmirch our colleagues' reputations by criticizing their work to their patients. With false pride and arrogance, or a lust for gain, a caustic comment is made, a question left unanswered, an eyebrow raised which leads, at the least, to the patient's loss of confidence in his doctor, possibly to court action, invariably to degradation of our professional prestige. Let's polish up the Golden Rule each morning, so that it gleams before us through the day.

Let's face these facts and the many others which all of us fall asleep on each night, and having faced them, let's do something about them.

Let's face the fact that we in medicine must awaken, take stock of ourselves; that each of us must pause to think. In the remoulding of medical practice that is upon us, surely there is opportunity, and need, to remould ourselves. Perhaps it is not too late to regain the place we held through the centuries, as far back, even, as the Book of Ecclesiasticus: "Honour the physician for the need thou hast of him; for the most High hath created him."

8 Prince Arthur St.,
Halifax, N.S.

CASE REPORT

HISTOPLASMOSIS WITH SARCOID-LIKE LESIONS OCCURRING IN MULTIPLE MYELOMA*

A. J. BLANCHARD, M.D. and
J. S. OLIN, M.D., *Toronto*

THE FIRST report of an autopsy on a fatal case of histoplasmosis occurring in Canada was made by one of us (A.J.B.[1]) in 1951. Since then, additional cases have been encountered, apparently with increasing frequency. In a recent paper, Haggar, Brown and Toplack[2] described seven cases occurring in Southwestern Ontario and reviewed the Canadian literature on the subject. This report describes an instance of histoplasmosis occurring in a male patient who also suffered from multiple myeloma. This individual, in addition, presented the diagnostic problem, during life, of granulomatous lesions in the bone marrow.

The patient, a 64-year-old Italian, had lived in Italy until the age of 31 years and in South America from 1923 to 1925. He then came to Canada and had lived in this country continuously since that time and was employed in the construction industry as a labourer. He was admitted to Sunnybrook Hospital, Toronto, on November 5, 1957, complaining of dyspnea, cough and fever of three months' duration. A past history was obtained of an illness, in 1943, characterized by distress in the right chest unassociated with cough. Roentgenograms at the time showed a dense shadow in the right lower lobe, and chest aspiration yielded dark blood-stained fluid. Exploration of the right chest was carried out. The lung was adherent to the chest wall throughout but no mass was found. It was the opinion of the surgeon that these changes were probably the result of an inflammatory process.

He was admitted to another hospital in March 1955, with the complaint of a radicular type of pain which had been present for one month, radiating from the upper spine to the right and left chest.

He had the additional complaints of dyspnea on exertion, and sweating. Urinalysis showed 4+ albumin and the presence of Bence-Jones protein. Sternal marrow smears had a very marked infiltration of plasma cells. Roentgen studies were carried out and compression of D4 and D7 vertebrae was demon-

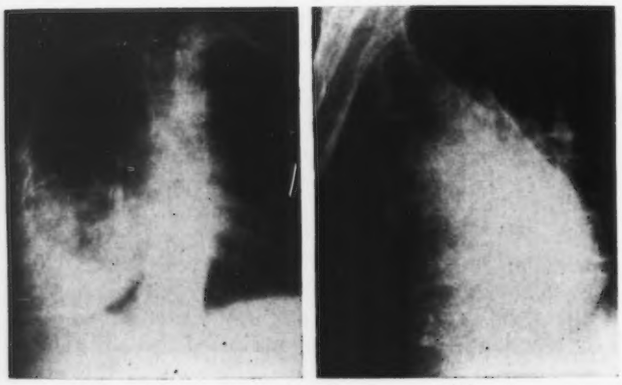
*From the Pathology Laboratory, Sunnybrook Hospital, Department of Veterans Affairs, Toronto.

strated as well as a mass in the right chest that was rimmed with calcium. Electrophoresis of the patient's serum revealed increased alpha$_2$ globulin and decreased gamma globulin. A prominent spike between the beta and gamma positions in the electrophoretic pattern of the urine was felt to represent an abnormal protein. The patient was treated with urethane, three to four grams daily, almost continuously for over 2½ years. The drug was discontinued temporarily in December 1955, for a few weeks, when a leukopenia of 2150 cells per c.mm. occurred. He was followed very closely and his clinical response was considered to be excellent.

A cough, productive of two tablespoonsful of mucoid sputum daily, with dyspnea and wheezing, worse in the morning, began in September 1957, accompanied by an episode of fever which then persisted for several months. The patient was admitted to Sunnybrook Hospital for investigation in November 1957. Functional enquiry revealed pain in the region of the left upper humerus, worse at night, that was relieved by change in position. Physical examination was done on this squat, pale individual who breathed rapidly and shallowly. There were signs of fluid in the lower right posterior and anterior chest cavity. Loud systolic murmurs were heard at the apex and aortic areas. The blood pressure was 118/76 mm. Hg. The tip of the spleen was readily palpable. The liver was not enlarged and no lymphadenopathy could be found. There was considerable upper dorsal scoliosis with slight loss of lumbar lordosis, but no bone tenderness was elicited.

Laboratory Investigation

Urinalysis showed the presence of albumin 1+, Bence-Jones protein and an occasional pus cell and hyaline cast. His white blood count was 3000 per c.mm. with 92% neutrophils, hemoglobin 63%, and sedimentation rate 115 mm. per hour. His serum calcium was 9.6 mg. %; alkaline phosphatase was 11.2 (Shinowara-



(a) (b)

Fig. 1 (a).—A penetrated film showing calcified right pleural mass. (b) A right anterior oblique film showing mass located predominantly posterolaterally.

Jones-Reinhart) units. A Congo-red test showed that 15.4% of the dye disappeared from the blood in one hour. The tuberculin and histoplasmin skin tests were negative. Serum protein fractionation values were albumin 2.73 g. per 100 c.c. and globulin 2.85 g. per 100 c.c. Electrophoretic studies of serum indicated reduced albumin with relative increase in alpha$_1$ and alpha$_2$ globulin and low gamma globulin. Examination of the urine by this method showed a prominent spike

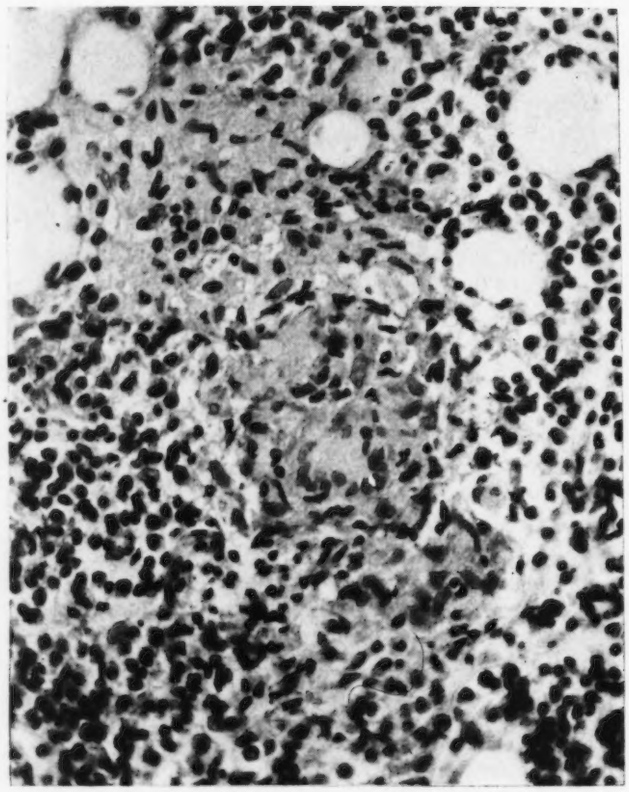


Fig. 2.—A granuloma in a sternal marrow aspirate obtained during life.

between the beta and gamma positions. (The results were almost identical to those of 1955.) Repeated cultures of sputum grew normal respiratory flora only; no acid-fast bacilli were seen. Blood cultures were negative. Roentgenograms showed a large, partially calcified pleural mass in the right lower chest (Fig. 1a and 1b). There were generalized demineralization of the bones surveyed and numerous compression fractures of dorsal and lumbar vertebrae, but no circumscribed osteolytic lesions were noted. Histological tissue sections of bone marrow aspirated from the sternum on November 15, 1957, contained large fragments of marrow with groups of plasma cells that varied in size and were closely packed together. As well, numerous granulomata composed of epithelioid cells and Langhans'-type giant cells were seen in the tissue sections (Fig. 2). Necrosis was noted in one small granuloma. No tubercle bacilli or fungi could be demonstrated with acid-fast or periodic acid-Schiff (P.A.S.) stains. Bone marrow smears showed large numbers of immature and mature plasma cells. The bone marrow was cultured for fungi and tubercle bacilli on November 18, 1957.

The hospital course was characterized by fever with a temperature of 99° F. in the morning and sharp increases to 101° F. in the evening during the first two weeks; then the fever levelled off at 102° F. Urethane was continued in doses of 3 g. daily and was discontinued on November 29 when the white blood count fell to 600 cells per c.mm. Prednisone and tetracycline therapy was initiated at this time. The discovery of granulomatous lesions in the sternal marrow created a diagnostic and therapeutic problem. The possible diagnoses considered included disseminated tuberculosis, sarcoidosis, a fungus infection or an unusual manifestation of multiple myeloma.

The patient developed severe pain in the mouth and frequent chills. The temperature rose to 104° F. (per rectum) and the pulse and respirations became rapid on December 1. Because of the possibility that the lesions might be tuberculous, therapy with streptomycin, para-aminosalicylic acid and isoniazid was begun on December 3, but the patient suddenly became anxious and dyspneic, and died on the following day.

Autopsy

The relevant findings were confined to the pleural spaces, lungs, mediastinal lymph nodes, heart, liver, spleen, adrenal glands, kidneys, bone marrow and vertebral column.

Gross findings.—The left pleural space was obliterated by fibrous adhesions that were broken down with some difficulty. The right pleural space contained extensive fibrous adhesions, and a large mass occupied the usual site of the middle and lower lobes. The mass was roughly pyramidal in shape, measured 10 x 11 cm., was fused to the chest wall and was removed only after very difficult sharp dissection. It was rimmed with a thin layer of brittle calcium. The cut surface of the mass was variegated, being grey, pink and red at foci of recent hemorrhage. It was diffusely friable with areas of caseous consistency. The mass compressed the right middle and lower lobes to such a degree that only a narrow strip of atelectatic lung remained. The appearance of the mass was that of an old encapsulated hematoma.

Both lungs showed a moderate degree of edema. The left lung weighed 600 g. and the right lung, with the attached mass, 1055 g. The mediastinal lymph nodes were prominent, and at the level of the carina a group of enlarged nodes was found which on section had a variegated caseous appearance and the usual deposits of anthracotic pigment.

There was generalized hypertrophy of the heart, which weighed 435 g. There was a slight degree of mitral stenosis, the orifice admitting 1½ fingertips, and there was a moderate degree of aortic stenosis.

The liver was slightly increased in size, weighing 1715 g. The spleen was enlarged, weighing 375 g., and was firmer than usual. The adrenal glands were slightly enlarged, their combined weight being 20 g. The right adrenal gland was removed with difficulty because it was surrounded by fibrous adhesions that bound it to the liver. Areas of caseation were present in both adrenal glands. This caseation was most marked in the right adrenal. The kidneys were enlarged, the right weighing 195 g. and the left 225 g.

The bone marrow of the sternum, one of the lumbar vertebrae, the left ala of the ilium, and the left femur were red with mottled grey and pink areas. The vertebrae were moderately osteoporotic. There was marked flattening of the bodies of the third to fifth lumbar vertebrae. No areas of tumefaction were seen.

Microscopic Examination

Several sections of the lungs were examined which showed fibrous thickening of the pleura and occasional collections of mononuclear cells distended with intracellular organisms. These organisms had the typical appearance of *Histoplasma capsulatum* and they appeared as minute, rounded structures surrounded by an unstained capsule. A few focal clusters of staphylococci were seen. The right pleural mass was composed of eosinophilic, amorphous, granular material with channels containing red blood cells. There was a patchy, fine, granular calcification and some clusters

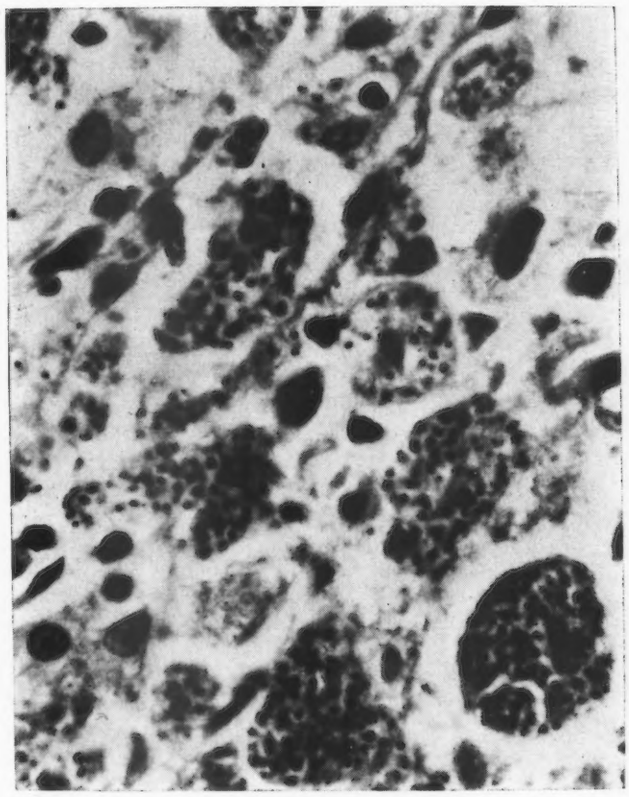


Fig. 3.—Intracellular site of *Histoplasma capsulatum* in an adrenal lesion. P.A.S. stain.

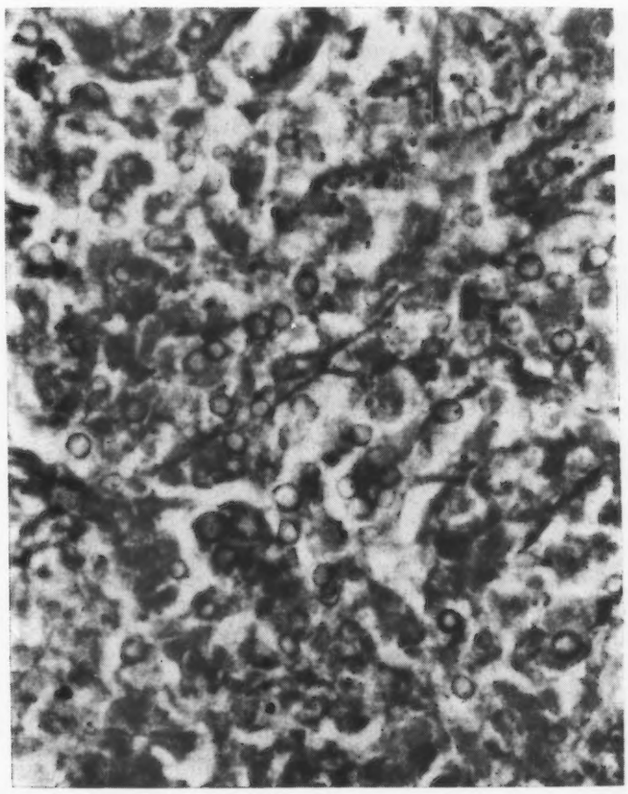


Fig. 4.—An extracellular site of *Histoplasma capsulatum* in an adrenal lesion. P.A.S. stain.

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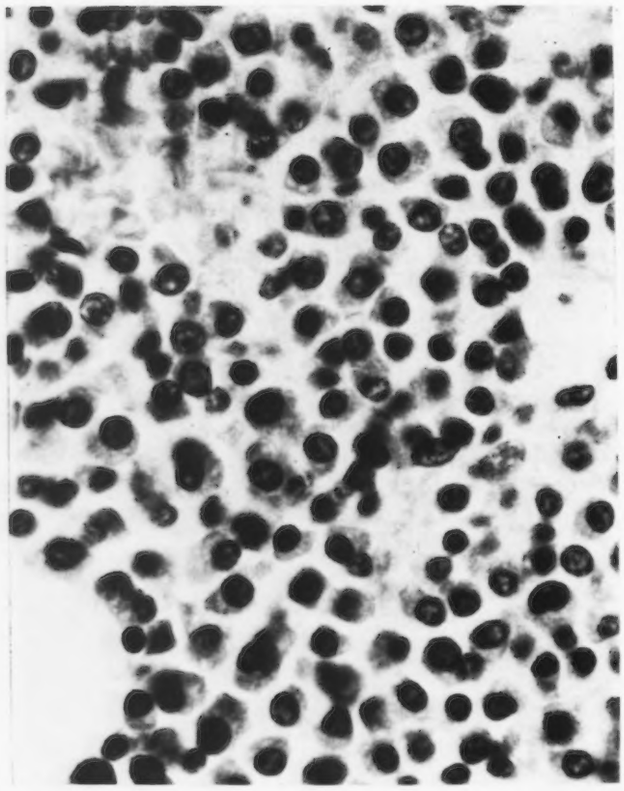

Fig. 5.—A specimen of bone marrow at autopsy showing a mass of plasma cells.

of cholesterol crystal clefts. No organisms were identified in the mass. The periphery of the mass was bordered by dense, hyalinized, partially calcified fibrous tissue. Adjacent to this, the lower lobe of the right lung was completely atelectatic.

The mediastinal lymph nodes contained multiple, old granulomata, some with necrosis. In these necrotic foci, rounded, extracellular, P.A.S.-positive bodies were seen, and were considered to be consistent with the extracellular form of Histoplasma.

The liver showed slight fatty change, and foci of partially necrotic granulomata were noted in which macrophages containing Histoplasma were seen. Occasional mononuclear cells distended with Histoplasma and also clusters of staphylococci were found in the spleen.

The adrenal glands showed myriads of Histoplasma contained within distended macrophages. These were easily visible in hematoxylin and eosin stained sections but were demonstrated to better advantage with the P.A.S. stain as dark red bodies surrounded by an unstained halo (Fig. 3). There were extensive areas of caseous necrosis and granuloma formation, and scattered within these areas of caseous necrosis were the extracellular forms of Histoplasma. These appeared as spherical bodies taking up the P.A.S. stain and measuring approximately 10-12 micra in diameter. They varied in size and were appreciably larger than the intracellular form of the organism (Fig. 4). The central punctate red staining bodies often described were not seen in most instances.

The kidneys showed an occasional necrotizing granuloma in which Histoplasma were seen with the P.A.S. stain. Small focal collections of the organisms were also seen within the interstitial tissue of the medulla. Some of the organisms were apparently lying free, whereas others were contained within macrophages.

Samples of bone marrow taken from several sites showed irregular sheets of closely packed plasma cells in all sections (Fig. 5). The extent and compactness of these masses of plasma cells were considered to be indicative of myeloma. In the bone marrow, necrotizing granulomatous lesions were also present and in these, organisms resembling Histoplasma could be seen with the P.A.S. stain.

Bacteriology and Mycology

Cultures were carried out by Dr. Marion Ross (Bacteriologist, Sunnybrook Hospital) from sternal marrow tissue taken during life and from various tissues obtained at autopsy. *Histoplasma capsulatum* was cultured from the bone marrow taken during life and from bone marrow, adrenal gland and mediastinal lymph node obtained at autopsy. A very heavy growth of *Micrococcus pyogenes* var. *albus* was obtained from the autopsy tissue as well, indicating a terminal staphylococcal septicemia.

DISCUSSION

One can only speculate about the significance of the chest lesion investigated in 1943. The mass and bloody pleural fluid were consistent with an inflammatory lesion, possibly histoplasmosis.

The diagnosis of multiple myeloma might be questioned in this case. However, the clinical and laboratory findings fulfilled the criteria usually accepted as diagnostic of that condition. The persistently abnormal serum and urinary proteins, especially the presence of Bence-Jones protein, are in favour of that diagnosis. The clinical picture with bone pain, osteoporosis and excellent response to urethane is in accord with the diagnosis of myeloma. The bone marrow smear taken in 1955 showed marked plasma cell infiltration with many immature forms. This was confirmed in 1957 by the finding of sheets of plasma cells in the bone marrow sections. It would be most unusual to find this number of plasma cells in a reactive plasmacytosis, although levels as high as 55% in cases of sulfonamide sensitivity and 60% in acute agranulocytosis have been reported.[3]

A histoplasmin skin test was performed upon the patient during his final admission and a negative response was obtained. A standard, commercially available preparation was employed, taken from a vial which had been used previously (the date of expiration of potency was unknown). The criticism might be made that this histoplasmin was inert. Nevertheless, a negative skin test response could occur in this case, since the patient was febrile and in the terminal stages of disseminated histoplasmosis. This state of "anergy" is well known in the terminal stages of miliary tuberculosis and disseminated histoplasmosis and is considered to be indicative of a poor prognosis.

The relationship of histoplasmosis and malignant lymphoma has been commented upon by several authors[4, 7] who have noted the concurrence of the two conditions. Although multiple myeloma is not

a member of the malignant lymphoma group strictly speaking, it is a similar disorder so that a similar connection may exist. The authors have not found another instance recorded in the medical literature in which multiple myeloma and histoplasmosis have coexisted. The association might be explained in several ways.

The concurrence may merely be an unusual coincidence. This seems unlikely. The fungus infection may, in some way, have led to the development of multiple myeloma in this man. There is no evidence to support this theory.

Alternatively the fungus infection may have induced a cellular reaction similar to that seen in multiple myeloma. However, on evidence already presented, this is a true case of neoplastic multiple myeloma and not reactive plasmacytosis.

The most likely explanation is that the malignant transformation of the reticuloendothelial tissues altered the host's ability to deal with the fungus infection. An additional factor which may be of significance is the change in the plasma proteins.[8] The low level of gamma globulin, in which antibodies are contained, may have allowed the dormant fungus infection to become active. In this case there may have been a primary focus in the lung, possibly in the right lower lobe and pleura, with secondary spread to the hilar lymph nodes. The infection had become arrested and remained so until the development of malignancy of the reticuloendothelial system and the associated changes in the plasma proteins.

The tissue reaction that is usually considered typical of histoplasmosis is a diffuse accumulation of histiocytes containing within their cytoplasm large numbers of *H. capsulatum*. Areas of caseous necrosis may also be found. However, other types of tissue reaction may occur.[9] Epithelioid-cell granulomata resembling the lesions of tuberculosis or, in some instances, Boeck's sarcoid have been described. At times, large circumscribed fibrocaseous nodules have been encountered in the lung which may throw a "coin" shadow in the radiograph and, in the absence of adequate study, may be classified by the pathologist as "tuberculomas".

A non-caseating epithelioid-cell granuloma, resembling the lesion of sarcoid, was seen in this patient's bone marrow sections obtained during life. This feature presented a diagnostic problem of considerable importance from the standpoint of therapy. No fungi or acid-fast organisms could be demonstrated in the granulomata by special stains in the biopsy material, although *H. capsulatum* was later recovered in culture. At postmortem examination 17 days after the sternal marrow biopsy, no granulomata similar to those seen during life could be found in the marrow but miliary, necrotizing foci were present in which histoplasma were readily seen. An overwhelming proliferation of histoplasma may have occurred terminally and, as a result, the granulomata had undergone extensive necrosis obliterating the sarcoid-like tissue pattern.

There are many reports in the literature concerning the relationship of histoplasmosis and sarcoidosis.[10, 11, 13] Cases are detailed which fulfil the criteria required for a diagnosis of sarcoidosis but subsequent investigation has revealed the presence of histoplasmosis. In these cases it is difficult, if not impossible, to determine whether sarcoidosis had been present from the beginning and histoplasmosis had occurred secondarily, or if the presence of Histoplasma infection had induced a tissue reaction and a clinical and biochemical picture indistinguishable from sarcoidosis. Symmers[13] has reported a case with the clinical features of sarcoidosis and biopsy confirmation followed by apparent spontaneous regression. The subsequent development of enlarged lymph nodes led to further biopsy which revealed obvious Histoplasma infection. Although he felt that two distinct disease processes were present, the possibility that the original illness was a manifestation of histoplasmosis was considered. Pinkerton and Iverson,[11] reviewing cases diagnosed as sarcoidosis at the Armed Forces Institute of Pathology, Washington, D.C., found three cases of disseminated sarcoid lesions in patients with histoplasmosis.[11] They pointed out that a fundamental point of difference between histoplasmosis and sarcoidosis is the fact that many patients with histoplasmosis die of adrenal insufficiency because of extensive adrenal involvement, but in true sarcoidosis adrenal involvement is rare. Current interest in the etiology and nature of sarcoidosis is high. A conference on sarcoidosis was held in 1956 which advocated that a registry of cases be established to collect information on etiology.[12] If a review were made of cases previously called sarcoidosis and the tissue sections were stained for fungi, further cases of histoplasmosis might be uncovered.

SUMMARY

A case of disseminated histoplasmosis with sarcoid-like granulomatous lesions has been described which occurred in association with multiple myeloma. The relationship of the two conditions has been discussed. The tissue reactions that may be found in histoplasmosis have been reviewed and special mention has been made of the possibility of confusing, on histological examination, the granulomatous lesions of histoplasmosis with those of sarcoidosis.

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CURRENT VIEWS ABOUT SEAT BELTS

FOR MANY years the automobile seat belt has been advocated to reduce injury and death associated with accidents involving the vehicle and its passengers. The risk of injury and death is, to a large extent, dependent on the frequency of ejection of the passenger from the vehicle at the time of the accident. Two other major variables that affect both the frequency of passenger ejection and the risk of injury are the severity of the accident and the seat position occupied. In one study of accidents which produced injury, 13.6% of adult occupants were ejected and the fatality rate was five times greater in this group than for occupants who were not ejected. This study, conducted in the years 1953-1956, led to the conclusion that the prevention of passenger ejection alone would result in a 25% reduction in accident mortality. More recent investigations carried out since 1956, when improved door-locks became standard in most American cars, suggest that this simple modification has reduced the risk of occupant ejection by about 48% and that of dangerous injuries by 29%.

For those passengers who remain in the vehicle, the magnitude of deceleration determines the degree of injury and risk of death. The forces which develop during deceleration are measured in G's (one gravitational unit equals one pound of force divided by one pound of mass), and indicate how much restraining force is required to keep the individual in his seat. In a rapid descent in an aircraft, the pilot may lose consciousness after 7G or more have developed. A 200-lb. man travelling in an automobile at 40 miles per hour will develop 1G in coming to a full stop over a distance of 60 feet, 5G in stopping over a 10-foot distance and as much as 20G in violent collisions. These tremendous forces are dissipated in two to three seconds and it is probable that, if it holds during part of this period, the seat belt will offer considerable protection.

Nevertheless, as Frazier[1] has recently pointed out, seat belts are not a universal remedy equally applicable to the many diverse forms of injury to which the motorist and passengers are exposed. One study of seat belt effectiveness compared injuries among 933 operators and occupants of the right front automobile seat who used belts, with those of 8784 drivers and occupants of this position who did not. Those who used seat belts sustained 35% fewer "major-to-fatal" injuries than non-users. The rate for "any injury" was about the same in both groups, but in each seating position that was examined, the use of seat belts reduced the proportion of the "major-to-fatal" grade of injuries. Further analysis, including the relationship of the colliding vehicles at the moment of impact, showed that the expected and observed number of major-to-fatal injuries in front-front and front-rear accidents were almost identical among occupants with and without seat belts, whereas in rollover and angled-impact accidents, the observed total of major-to-fatal injuries in belt-users was less than half of that in the group without belts. Evidence from simulated accidents indicates that the restraint from seat belts provides negligible protection against injury, under severe conditions, because there is insufficient clearance between the head and chest of the front seat occupant and the interior structures of the car. However, only about 33% of accidents are of front-to-front or front-to-rear types; 20% are rollovers, and the remainder are angled or lateral impacts. Rollover and angled or lateral impacts result more frequently in ejection, and it is here that the seat belt plays its greatest role in passenger safety, as it provides the best protection currently available against ejection during impact and against violent dislocation within the automobile.

The average reduction of 35% in major-to-fatal injuries is based upon the experience with the operator and occupants of the front seat. Rear-seat occupants have far less risk of ejection and their accident fatality rate is about one-half that of front-seat occupants. The lesser incidence of serious or fatal injuries among children passengers is related, in part, to the frequency with which they occupy the rear seat.

All physicians writing on this subject do not agree that seat belts should be worn. In this connection it has been observed that a passenger, held fast in his seat at the time of collision, is at a temporary disadvantage in certain emergency situations such as those created by fire, or immersion after an accident. However, as pointed out by Atkinson,[2] only 0.2% of injury-producing accidents are followed by fire and only 0.3% by immersion, and fixation is a risk much to be preferred to ejection at the moment of impact. Further, the seat belt should make it possible for the individual to cope with these emergencies more effectively by surviving the impact with less serious injuries.

The alleged liability to increased risk of whiplash injuries to the cervical spine, among those wearing seat belts, applies chiefly to those individuals involved in rear-end collisions. This as yet unassessed hazard may be a contraindication to the use of the lap-strap, especially those that are combined with a shoulder or diagonal restraint, but higher and better designed seat-backs may decrease the risk of this complication. The lap-strap alone, particularly in automobiles of small dimensions, would give no protection against body-flexion and jack-knifing, for even at an impact speed of 21 m.p.h., the restrained body has a forward head movement of about 28 in. Thus, some form of body restraint, as well as hip restraint, is essential.

The details of design of the seat belt are of importance because an impact as low as 21 m.p.h. produces a maximum lap-belt load of 5500 lb. and this formidable strain develops within 70 to 100 milliseconds. Some of the requirements of an adequate seat belt are outlined by Severy, Mathewson and Siegal[3]. Instead of a three-inch-wide seat belt, tested under a stress of 3000-4000 lb., which is currently used by British motorists, they recommend a three-inch-wide nylon lap belt made from material which will stand a strain of 8000 lb. This belt will increase motorist protection by: (a) reducing contributions to slack such as those resulting from belt stretch and body deformation; (b) reducing restraining unit pressure applied by the lap belt to the motorist because of the greater surface area provided by a three-inch belt; (c) providing a restraint by a belt with a strength more in keeping with the stresses encountered in automobile accidents and therefore less likely to fail during impact; (d) reducing front seat occupants' leg injuries by reducing belt elongation that permits the knees to strike the dashboard during moderately severe front-end collisions. A full harness, including a lap-strap worn with no slack, would be ideal but in many cars would restrict driver movement. Atkinson has in use an 8000-lb. strength, combined lap and diagonal belt, with anchorage points strengthened by 3″ x 1/8″ steel plates, which permits unhampered driver control and provides increased passenger comfort and safety, particularly for children.

In a recent investigation in the United States[4] that involved the testing of 41 seat belts purchased at random in retail stores, it was found that only nine met Federal specifications. The belt and its assembly was subjected to a stress of 5000 lb.; i.e., it would hold a 200-lb. man in his seat during a 25-G impact without breaking. The car itself will probably disintegrate around the passenger at about 20G. All the belts which resisted a tension of 4000 lb. had all-nylon webbing. The cost of these belts, in this survey, ranged from $10.30-$12.95 per belt, with installation costs from $9-$15 for a set of two. The belt assembly should be anchored through the car floor, preferably to the steel frame, because many car floors are of light construction.

The official position of the Canadian Medical Association is clear; it has recommended the use of seat belts in automobiles in its approval of the reports of the Committee on the Medical Aspects of Traffic Accidents in both 1960 and 1961. Shortly after the latter meeting, the American Medical Association in co-operation with the National Safety Council, the U.S. Public Health Service and other agencies launched a nation-wide program to persuade American automobile owners to use seat belts.

Only experience will show which types of seat belts should be recommended for general use, from the points of view of safety, realistic cost, convenience and adaptability to standard automobile brackets. However, lives will not be saved, even those represented in the 35% of accidents of the rollover and angled impact type where the seat belt is most effective, unless large numbers of the profession, and the public at large, accept these devices as necessary and wear them at all times. In one survey in the United States it was estimated that less than 1% of automobile operators had safety belts installed in their vehicles. In 2000 belt-equipped cars that were involved in collisions, the seat belts were not in use in almost 70% at the time of the accident. It should be stressed that seat belts *are* required for local driving; the risk of "local hops" is reflected in the fact that in 1958, 47% of all deaths occurred at travel speeds below 40 m.p.h. and 66% took place within 25 miles of the driver's home.

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SIR AUSTIN BRADFORD HILL

THE LIST of the Queen's Birthday Honours published on June 10, 1961, contains the names of 46 physicians whose services to the Crown have been suitably recognized. Many members of the Canadian medical profession will recognize former teachers, valued colleagues and, perhaps, even wartime comrades in the lists. In addition, the Journal is glad to join with the *Lancet* in adding a special word of congratulation to Professor A. Bradford Hill on his knighthood. We can do no better than quote the felicitous phrases of our British colleague, "Hardly anyone now remembers that Professor Bradford Hill did not actually take a medical degree. In his hands, statistics have generally seemed an expression of common sense, and it is by helping so many people think more clearly that he has done so much for medicine."

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PRIMARY MYELOID METAPLASIA

MYELOSCLEROSIS is one of a group of conditions which are now known as "myeloproliferative disorders". The common denominator in all of these is a disorderly proliferation of hematopoietic cells beyond physiological demand, and a variety of intermediate forms between the extremes of myeloid leukemia and myelosclerosis has been recognized.[1] This spectrum of disorders of overlapping clinico-pathological patterns derives from a proliferative process which affects several cell lineages at various stages of their development and involves them to differing degrees. This process, playing upon a complex system of cell types, gives rise to a number of puzzling clinical patterns.

Two hypotheses have been advanced to account for the sclerosis of the bone marrow and the myeloid metaplasia of the spleen, liver and sometimes of other organs which accompany it. The older, first advanced by Donhauser in 1908, is that the marrow was replaced by fibrous tissue or bone, after which myeloid metaplasia arose in compensation by a process analogous to the extramedullary hematopoiesis in pernicious anemia. An alternative view is that the proliferative stimulus affects various cell lines all derived from the "primitive mesenchymal cell", including the fibroblasts and the osteoblasts as well as hematopoietic cells.[2] According to this concept the marrow and extramedullary changes proceed simultaneously and are more readily recognized at an early stage in the extramedullary sites where the presence of proliferating cells is more conspicuous. This concept of "benign multifocal neoplasia" led to the introduction of the term "agnogenic"* myeloid metaplasia by Jackson, Parker and Lemon[3] when they reappraised this syndrome in 1940.

More recently the entire concept of myelosclerosis has been re-explored by Bowdler and Prankerd[4] in an intensive study of 16 patients showing histological evidence of myeloid metaplasia of unknown origin. Radioactive isotope studies on many of these patients are reported in a separate communication.[5] On the basis of these investigations the wide variation in the clinical and hematological features of these cases was attributed to the variable degree to which the individual cell lines are involved. The patterns of presentation in the 16 cases included bone marrow failure ("aplastic anemia") with hepatosplenomegaly (five), polycythemia (three), leukocytosis (one), thrombocythemia or megakaryocytosis (four) and hemolytic anemia (three). The validity of the concept that these variable clinical manifestations represent a single disease entity was carefully examined. The following observations of interest emerged in the discussion of this intriguing study: (a) *myeloid metaplasia may precede the marrow fibrosis*; (b) the fibrous proliferation may be well developed in the spleen and liver and not confined to the marrow, suggesting the presence of a generalized fibroproliferative tendency; and (c) the frequent occurrence of myeloid metaplasia with excessive production of erythrocytes, leukocytes or platelets does not suggest that it is arising as a response to a deficiency of cell formation. These observations prompted the proposal that the term "primary myeloid metaplasia" be adopted to designate such cases in preference to "myelosclerosis", since it more accurately denotes the underlying disorder.

This concept of primary myeloid metaplasia may help the physician to deal with such vexing problems as the significance of the elevated erythrocyte or leukocyte counts in patients with these disorders. Are they to be regarded as early or aberrant forms of polycythemia or chronic myeloid leukemia and treated as such? Are these conditions varieties of the disease, primary myeloid metaplasia, in which undue attention is directed to the peripheral blood picture? The value of distinguishing, as a clinical guide, those cases showing myeloid metaplasia is considerable. First, the diagnosis rests on a clear pathological basis and may be made by splenic puncture, liver biopsy and occasionally by lymph node biopsy. If a hemorrhagic tendency or other contraindications preclude the use of these techniques, isotope studies provide an alternate diagnostic method. Secondly, diagnosis defined in terms of the examination of peripheral blood smears only may require frequent revision during the course of a single case while the underlying tissue changes have altered but little. Thirdly, this diagnosis will draw attention to the possible sequelae which may follow in the wake of primary myeloid metaplasia, notably hemolytic anemia, marrow failure, a marrow unresponsive to hemorrhagic stress or hemolysis and the consequences of unrestricted cellular proliferation of one or more lines of hematopoietic cells. This diagnosis, when made, is a relative or absolute contraindication to certain forms of therapy used in other diseases that simulate chronic myeloid metaplasia, e.g. splenectomy in acquired hemolytic anemia and irradiation of the spleen in chronic myeloid leukemia. It was reported in one review[6] of this disorder that of 27 patients who were subjected to splenectomy, 15 died within a few days of operation. Irradiation of the spleen is rarely of material benefit and is often followed by serious deterioration in the patient's condition.

These concepts appear to constitute a useful contribution to the classification of a difficult and not uncommon problem in general medicine.

*Of unknown or uncertain etiology.

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Letters to the Journal

THE POSITIVE SIGNS OF NEUROSIS

To the Editor:

Dr. T. F. Rose in the May 20 issue of the Journal (*Canad. M. A. J.*, 84: 1132, 1961) gives an account of his experience with "neurotic" patients who seek medical advice for somatic ailments. He describes as "positive signs of neurosis" some behavioural patterns in these patients and proposes that these be taken as the diagnostic criteria of a neurotic illness (thus dismissing the significance of their somatic symptoms).

I would like to take exception to this point of view. The proposed diagnosis for neurosis is not psychiatrically correct and, furthermore, the grouping together of all psychogenic symptoms as "neurotic" is not beneficial for either the patient or the doctor.

Neurosis is not usually defined by malingering, histrionic or socially unacceptable behaviour. It is the rigidity, repetitiousness, unadaptability and unrealistic character of behaviour which is typical of neurosis plus the fact that it is determined not by the demands of a real situation but largely by unconscious motives. Neurotic illnesses are specific psychopathological processes which should be distinguished from the general groups of mental disturbances.

The diagnosis of somatic symptoms related to psychiatric conditions should not rest so much on the waiting-room behaviour of the patient, as Dr. T. E. Rose suggests, but on definite criteria which indicate the exact origin of these symptoms.

Psychogenic symptoms often present a great diagnostic challenge to the physician. Unfortunately, the general tendency is to make the diagnosis by exclusion of all organic diseases which could be responsible for such symptoms. I agree with Dr. Rose that this is an expensive, time-consuming and unscientific attitude which should be abandoned. However, the practice of diagnosing psychogenic symptoms by eliminating physical diseases should not be replaced by the equally incorrect practice of labelling every such symptom as "neurotic" once some criteria of neurosis have been identified (wrongly or rightly) in the behaviour of the patient. Neurosis, as such, does not produce somatic symptoms, except for the hysterical conversion ones.

The great majority of functional symptoms represent the physiological correlates of various emotional states, usually tension-anxiety and depression. These symptoms are mostly mediated by the autonomic nervous system, although evidence has accumulated indicating that all organ functions can be altered by a strong emotional state. Tachycardia, increase in blood pressure, increased perspiration, dryness of the mouth, gastric malaise, dyspnea, muscular spasms, nausea and vomiting, diarrhea are some of the commonly identified pathophysiological correlates of anxiety states. The behavioural characteristics and ideational content of anxiety are present at the same time and these, with a positive psychosocial history of precipitating events, should complete the picture of an anxiety tensional state which may or may not be the manifestation of a neurotic illness. The diagnosis of neurosis, however, requires additional criteria.

Depressive states are the second most common conditions for which a patient presenting "non-organic" symptoms may seek medical advice. Fatigue, paresthesias, muscular aches, constipation and gaseous distension, anorexia, loss of potency and sexual desire, menstrual disturbances and finally persistent headaches are the most readily identified somatic correlates of depression. As in the case of anxiety, the affective component of the depression and the positive history of specific precipitating events should be sought for a positive diagnosis. Depressive states are especially frequent in middle and late life.

Hysterical conversional symptoms (purely neurotic in origin), despite common belief, are relatively infrequent. Their diagnosis should rest upon the identification of the specific symbolic content of the somatic symptom and not upon the exclusion of an "organic" disease. Conversion symptoms are not simple equivalents of anxiety but the symbolic representations, in terms of somatic functions, of psychic conflicts.

Finally, the so-called "psychosomatic" diseases (organic illnesses in which the emotional-experiential factor constitutes an important but not the only determinant) should not be confused with the neuroses. A neurosis or psychosis or a character disorder may coexist with these conditions, but this coexistence does not signify a cause-and-effect relationship.

It is a fruitless oversimplification to regard all psychogenic symptoms as "neurotic" and so dismiss their value. They can often mask a severe emotional illness as in the case of an involutional depression, or they may be the only symptoms a patient can allow himself to show in a severe anxiety state. Correct understanding of these symptoms may lead to early diagnosis of the underlying cause and so save the patient from much suffering and financial hardship.

Since the general practitioner is the one who comes first in touch with the patient, his approach to the patient's symptoms has often a decisive effect on the course of the disease. Understanding of the psychogenic symptom is as important and mandatory for the physician as the understanding of the "organic".

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CONCERNING THE "BRITISH NATIONAL FORMULARY"

To the Editor:

After reading the recent correspondence concerning the excellent "*Medical Letter*", I am prompted to bring to your attention the "British National Formulary: 1960 (Alternative Edition)". This hard-bound pocket-sized reference book is obtainable through the British Medical Association, London, England, at a cost of a little more than $1. It can be recommended as a very useful aid to practice in Canada.

The "*Medical Letter*" is not, as yet, comprehensive. The widely used "Vademecum" is understandably orientated to the proprietary products of the sponsoring

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firms. The prescribers' information contained in it is often inadequate, and cannot always be accepted uncritically.

Prescribing by "proper" name appears now to be an uncommon practice. This is surely unfortunate, for it is a valuable discipline for both doctor and druggist. Moreover, provided official standards are complied with, it should be axiomatic that the most economical preparation be dispensed. As is well known, the price of equivalent brand preparations often varies widely.

The B.N.F. contains concise and authoritative monographs on established drugs; and is comprehensive for general practice. Preparations are listed by official titles: proprietary equivalents are given, and are largely applicable to Canada.

One final point: Why not a Canadian National Formulary?

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MEDICAL NEWS IN BRIEF

A NEW FERTILITY TESTING TAPE

In two Letters to the Editor in a recent issue of the *Journal of the American Medical Association* (176: 552, 1961), a description of a new testing tape impregnated with glucose oxidase and peroxidase is given. This tape will turn from pink to blue in the presence of glucose. In the cervical mucus, the glucose is alleged to be derived partly from the follicular fluid, though the possibility that some glucose may be derived from glycolysis within the fundus and cervix is postulated. The tape is inserted in a special vaginal applicator and if, after three minutes in the vagina, it turns blue, the woman is presumed to be in "the fertile phase of the menstrual cycle". One correspondent objects to advertisements which recently appeared in the Los Angeles *Times* which seemed to recommend this technique as an accurate method of contraception as well as conception, since this device was said to aid determination of ovulation time in the human. In defence of the tape, a second correspondent said that its primary use was to aid the childless wife whose basal thermal shifts are often difficult to interpret. Ovulation may occur three days before and three days after the day of lowest temperature. Individuals practising the "rhythm method" of contraception are instructed to avoid all coitus before and during the fertile phase as indicated by the appearance of a blue colour in the tape, and for at least three negative (pink) days after. Most of the 12 unwanted pregnancies, in over 65,000 occasions in which the test tape was used, occurred in couples who had coitus before the blue reaction phase of the cycle, or during the known mid-summer humidity and heat which affected the tape before it was wrapped in tinfoil.

STATUS OF VACCINATION AGAINST POLIOMYELITIS

Although the use of the Salk-type vaccine has had great impact on the incidence of paralytic poliomyelitis in the United States and other countries since 1955, there are still important problems associated with formalinized vaccine: (1) in many areas half the population under 40 years remains unvaccinated; (2) preschool-age children, a highly susceptible group, have had a low vaccination rate, and the percentage of those adequately vaccinated has been much lower than that among school-age children; (3) in the preschool-age group, antibody responses have been relatively poor in some instances.

The immunologic principle underlying the use of a live vaccine is obviously different from that involved with the killed variety in that the former induces an actual infection, although a very mild one, which is generally accepted as producing a more solid type of immunity than the injection of a non-living antigen. However, as Paul (*New England J. Med.*, 264: 651, 1961) points out, the use of live poliovirus vaccine presents certain major problems also, namely, those of safety, efficacy and methods of administration. The assessment of the safety of live poliovirus vaccine is based on certain stated laboratory criteria and on evidence derived from field observations. The capacity of live vaccine to immunize man has been assayed by at least two methods: (1) serologic surveys to determine the rates of post-vaccinal conversion from antibody negative to positive, the antibody titre achieved, and the degree of enhancement of already existing antibodies; and (2) field evidence of post-vaccinal immunity based on rates of clinical poliomyelitis in previously orally vaccinated groups as compared to appropriate control groups. Other features of live poliovirus vaccine requiring further assessment include: (1) their capacity to spread (intrafamilial and community spread); (2) their reactions and contraindications; (3) problems of manufacture; and (4) administrative schedules and plans.

In view of the increasing number of encouraging reports that have accumulated over the last two years, Paul believes that it is now more than likely that when oral poliovirus vaccine becomes available, it will be widely used in the United States in the future.

DIABETES MELLITUS IN THE AFRICAN IN RHODESIA

In a study by Gelfand and Carr (*Central African J. Med.*, 7: 41, 1961) of the nature of diabetes encountered in African patients from Salisbury, Rhodesia, and its surrounding area, the socioeconomic background of these patients showed that most of them came from groups who worked within the European economy, and whose traditional diet had been altered to include more foods containing, in particular, refined sugar and fats. There was also a group of older patients who made less use of these added foods. Thus, there appeared to be two types of diabetic: the more elderly diabetic who developed the disease irrespective of diet or

social status, and the young or middle-aged diabetic who probably came from a family with a latent diabetic trait, and whose dietary habits and rising social status appeared to have some bearing on the development of the disease. In only one case was there a family history of diabetes.

The clinical types of diabetes encountered in this study corresponded very closely to that of the European pattern; no variants such as "J" or "K" types were found. The symptoms appeared to be the same for the African and European, the main features being thirst, polyuria, weakness, weight loss and pruritus vulvae. The complications showed certain differences, notably the infrequency of pulmonary tuberculosis, pyogenic infections, gangrene, intercapillary glomerulosclerosis, retinochoroiditis and neuropathy. The insulin requirements for stabilization appeared to be high, compared to European requirements; this might have been due to the African's lack of understanding of the necessity to follow a strict dietary regimen. On the other hand, the level of blood sugar was found to be higher than in a European group, and this might have accounted for the difference in insulin requirement. It was also found that if the insulin requirements were exceeded, hypoglycemic coma readily developed.

There is a lower incidence of diabetes mellitus in the African than in the European. This might be a result of a greater resistance to change of the African's endocrine organs. Africans apparently have fewer endocrine disorders than Europeans.

SERUM MAGNESIUM LEVEL IN ACUTE AND CHRONIC RENAL DISEASE

The clinical signs of magnesium imbalance are difficult to evaluate, as this condition is usually associated with other abnormalities of water and electrolyte metabolism. Experiments have shown that hypomagnesemia produces tetany which is clinically identical to that of hypocalcemia. Hypermagnesemia leads to muscular weakness, absence of deep tendon reflexes and coma. The electrocardiographic changes are similar to those in hyperkalemia. Magnesium intoxication can occur through oral intake in the presence of impaired renal excretion.

The question has been raised whether magnesium retention is a factor in the symptomatology of uremia. In the reports published in the literature there is no clear relationship between the NPN and the serum magnesium level in uremic patients.

Losse and Koenig (*Deutsche med. Wchnschr.*, 86: 824, 1961) undertook a study of magnesium metabolism in patients with acute and chronic renal disease. The serum magnesium level was determined photometrically with titan yellow reagent. In 33 healthy controls its mean value was 1.65 ± 0.24 mEq./l. Forty-six patients with renal insufficiency were studied, fifteen of whom had acute renal failure because of trauma, blood loss or intoxication. In this group 48 serum magnesium tests were carried out, and the mean level was 2.32 ± 0.72 mEq./l. During the stage of anuria or oliguria almost all patients showed an elevated serum magnesium level, which dropped as soon as adequate diuresis was established, and before a fall in the NPN level was apparent.

The 31 patients in the second group had chronic renal impairment due to glomerulonephritis or pyelonephritis. Seventy-three magnesium determinations in this group revealed elevated, normal and low levels, and the mean value was 1.89 ± 0.70 mEq./l. No correlation was found between the non-protein nitrogen (NPN) and magnesium levels, but there was a clear relationship between the latter and the output of urine.

These results indicate that in the anuric or oliguric stage of renal insufficiency, hypermagnesemia is to be expected, and replacement fluids and medications therefore should be free of magnesium. Clinical and electrocardiographic signs of hyperkalemia in the presence of a normal serum potassium level can be explained on the basis of hypermagnesemia. The administration of calcium will alleviate the toxic effects of magnesium on the heart and central nervous system, and hemodialysis will lower the serum magnesium level. There is usually no danger of hypomagnesemia with the latter procedure, as the protein-bound magnesium is not dialyzed.

"AUTOANTIBODIES": CAUSE OR EFFECT?

Autoantibodies are now being described in a great variety of diseases. In some diseases, such as syphilis, tissue destruction is involved which is obviously responsible for stimulating antibody formation. In other diseases, such as myocardial infarction and viral hepatitis, autoantibodies against heart and liver tissues, respectively, appear days or weeks after the acute process, and obviously have no pathogenetic role. In yet other diseases of less obvious origin, specifically the post-myocardial infarction syndrome and chronic biliary cirrhosis, antibodies to heart and liver, respectively, are found, but their role is not clear. It is clear, however, that the simple demonstration of an autoantibody in a disease of unknown origin tells nothing about its etiology. Proof that circulating antibody actually causes lesions must be its ability to do so when injected into a normal recipient, the classic passive-transfer experiment. A variety of experimental and clinical findings suggest that humoral "autoantibody" can damage only cells that are easily accessible, such as the formed elements of the blood and the vascular endothelium, but is unable to produce lesions in solid tissues, such as the thyroid gland, gastrointestinal mucosa and synovia of peripheral joints.

Less attention appears to be paid to reactions of the "delayed" or "hypersensitivity" type, among them contact allergy, the allergy that accompanies many bacterial, mycotic, and viral infections, and the rejection of solid vascularized tissue homografts. Experimental autoallergies affecting lens, uvea, central and peripheral nervous systems, thyroid gland, testis and adrenal gland appear to be delayed hypersensitivity reactions; they are clearly autoimmune, but apparently are not mediated by humoral antibody. An editorial in the *New England J. Med.* (264: 566, 1961) points out that exclusive attention to circulating autoantibodies may result in a failure to discover other mechanisms that, in some cases, may play a major etiologic part in diseases in which the etiology is, as yet, unknown. Unfortunately, there is no alternative to skin testing with its possible inherent dangers, since there is no generally accepted *in vitro* method for identifying the cellular event underlying delayed hypersensitivity. Perhaps when tissue culture methods become more widely applied to the investigation of diseases of unknown etiology, it will be possible to study adequately autoimmune phenomena in solid tissues.

(Continued on advertising page 26)

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MEDICAL FILMS

THE FILMS listed below are held in the National Medical and Biological Film Library and are distributed by the Canadian Film Institute, 1762 Carling Avenue, Ottawa 3, Ont. The evaluations have been prepared by Canadian specialists in the subjects of the films, under the Medical Committee of the Scientific Division of the Institute, which is headed by Dr. G. H. Ettinger.

Congenital Malformations of the Heart. Part 1: Development of the Normal Heart—1952; sound; colour; 15 minutes.

Produced by the University of Washington School of Medicine, Department of Medical Illustration.

Description.—The chick embryo is used to illustrate the earliest development of the primitive cardiac tube. The first irregular pulsations are observed; the formation of the atrium is seen, and then the formation of the cardiac loop. The balance of the film is an explanation by animated diagrams of the formation of the septa and partitioning of the heart, with development of the arterial trunks by a spiral aortic-pulmonary septal division of the truncus arteriosus. The fetal circulation is explained, then the changes occurring in the pulmonary circulation with closure of the foramen ovale at birth.

Appraisal.—The film requires pre-instruction, particularly in regard to visualization of torsion and relative shift of the four embryonic parts of the heart. The sino-atrial region is rather neglected, the septum sinus venosae not being mentioned. Though not too amply treated, this forms a good review of the prenatal development of the heart. Recommended for medical students in the clinical years and medical specialists. Unsuitable for non-medical audiences.

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to: University of Washington, Instructional Materials Center, Seattle 5, Washington.

Congenital Malformations of the Heart. Part 2: Acyanotic Congenital Heart Disease—1952; sound; colour; 13 minutes.

Produced by the University of Washington School of Medicine. Sponsored by Dr. and Mrs. Maimon Samuels and the National Heart Institute under the direction of Robert F. Rushmer, M.D., Department of Physiology and Biophysics.

Description.—Though normally there is no mixing of venous and arterial blood in the heart, situations do occur where this happens. Patent ductus arteriosus is explained by animated diagram. The heart sound of this condition is heard and the gross heart outline shown. An aortic septal defect and patent foramen ovale are treated in the same manner. Aberrant pulmonary veins are illustrated and interatrial and interventricular septal defects discussed. Cine fluoroscopy is used throughout.

Appraisal (1960).—This is a good teaching film illustrating the acyanotic cardiac malformations clearly and accurately. The film is up-to-date; colour and sound are good. Recommended for medical students in clinical years. Suitable for medical specialists, general practitioners, medical students in pre-clinical years. Unsuitable for others.

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to Film Center, University of Washington, Seattle 5, Washington.

Antiseptics in the Prevention of Cross Infection—1959; sound; colour; 12 minutes.

Produced by Verity Films for Imperial Chemical Industries.

Description.—The film opens with a statement of the problem of in-hospital infections. A return to a stricter standard of asepsis is advocated and an analysis made of the methods of cross-infection. The elimination of sources of infection is discussed. The antiseptic chlorhexadine is recommended in all situations involving prevention or treatment of infections, with Gram-negative organisms especially. Various examples are shown and the proper use of an antiseptic in the control of cross-infection is illustrated.

Appraisal (1961).—The film has some very good sequences, notably the demonstration case of the spread of bacterial contamination by bed-making, changing dressings and coughing. The method of floor dusting used could be improved, and the child should have been shown washing under running water rather than in a basin. The commercial tone is not too obtrusive. Presentation is clear and interesting. Mainly instructional. Recommended for general practitioners, medical students in pre-clinical and clinical years. Suitable for nurses, technicians and medical auxiliaries. Unsuitable for non-medical audiences, specialists.

Availability.—National Medical and Biological Film Library ($3.00). For purchase apply to Publicity Department, Imperial Chemical (Pharmaceuticals) Limited, Fulshaw Hall, Wilmslow, Cheshire, England.

The Faces of Depression—1958; sound; black and white; 28 minutes.

Produced by Robert Anderson Associates, Ottawa, Ontario.

Description.—This instructional film shows some of the multiple appearances to be found in depressive states. Dr. H. E. Lehmann of the Verdun Protestant Hospital, Montreal, discusses the variety of signs and symptoms encountered. Patients are seen in short interviews designed to bring these out. Where signs are masked, special danger occurs and the depressed state may be hard to recognize. There may be confusion also with intracranial conditions, examples of which are shown.

Appraisal (1959).—The manifestations of depressive states are well shown in the many patients seen throughout the film. It is especially valuable for the emphasis put on depression as a disease seen earliest in the general practitioner's office. Dating is not important; commentary is accurate, interesting and stimulating. Recommended for general practitioners, medical students in clinical years and nurses. Suitable for medical specialists.

Availability.—National Medical and Biological Film Library ($4.50). For purchase apply to: Robert Anderson Associates, Mountain Road, Hull, P.Q.

Myasthenia Gravis—1955; sound; colour; 25 minutes.

Produced by Sturgis Grant. Sponsored by the Myasthenia Gravis Foundation Inc. and Hoffmann-LaRoche Ltd. Technical adviser: Thomas C. Fleming, M.D.

Description.—The film begins by illustrating the variety of symptoms that characterize a case of progressing myasthenia gravis. The features of the disease are then emphasized by reconstructing a case history from the first isolated symptoms onwards. Incidence is dealt with and then the pathology is discussed, using animated diagrams. Diagnosis from history supported by the clinical effects of chemical tests is discussed. Differential diagnosis is itemized, after which treatment is described comparing the three currently used anticholinesterase drugs. Thymectomy is mentioned as still having an equivocal place in therapy. The film ends with further emphasis on early diagnosis and the importance of a high index of suspicion.

Appraisal (1960).—The panel felt that the primary purpose of the film was to produce an awareness of myasthenia gravis and that the subject was well covered, in an accurate and interesting way. It is up-to-date and without errors. Recommended for medical specialists, general practitioners and medical students in clinical years. Suitable for nurses. Unsuitable for others.

Availability.—National Medical and Biological Film Library ($6.00). For purchase apply to: Myasthenia Gravis Foundation Inc., 2 East 103rd Street, New York, N.Y.

THE NINETY-FOURTH ANNUAL MEETING OF THE C.M.A.*

SCIENTIFIC PROGRAM: TEACHING SESSIONS

Wednesday, June 21

"THE MANAGEMENT OF URINARY INFECTION"

Chairman: *Dr. J. M. Campbell,* Saskatoon
Panelists: *Dr. D. G. Cameron,* Montreal
Dr. H. Medovy, Winnipeg
Dr. R. D. Jeffs, Toronto

Attention was directed to many aspects of the currently important subject of urinary infection, amongst which were: (1) the proper urine specimen, (2) the risk of radiation exposure with intravenous and retrograde pyelography, (3) vesicoureteral reflux, (4) quantitative studies of bacteriuria, (5) treatment of acute urinary tract infection, (6) urosepsis in diabetics, (7) hypertension and pyelonephritis, (8) urethral dilatation and (9) renal biopsy.

Opening remarks by all participants stressed the need for careful urinalysis, which requires a urine specimen properly collected under standard conditions and delivered as soon as possible to the laboratory for culture, routine and microscopic examination. The physician should personally examine the specimen, particularly microscopically. Ability to recognize various casts is of great importance. Emphasis was placed on the early detection of polymorphonuclear cell casts in pyelonephritis and of red blood cell casts in glomerulonephritis.

Regarding the risk of radiation injury from intravenous and retrograde pyelography, it was stressed that such examinations should be performed only with proper indications and properly standardized machines, and interpretation should be by well-qualified individuals to avoid unnecessary repetition. DR. H. MEDOVY, Professor and Chairman, Department of Pediatrics, University of Manitoba, indicated that he orders an I.V.P. (intravenous pyelograph) with the first urinary infection in a male child but with the second infection in a female. Dr. J. M. Campbell, Assistant Clinical Professor of Urology, University of Saskatchewan, added that when hematuria is present with a first infection in either male or female, an I.V.P. should be taken. Dr. D. G. Cameron, Physician-in-Chief, Montreal General Hospital, and Professor of Medicine, McGill University, referred to Professor Mayer's remarks regarding the use of x-ray radiation in pregnant women and re-emphasized the importance of avoiding unnecessary x-ray examination of the urinary tract.

Vesicoureteral reflux is often noted in cystograms of children who have recurrent urinary infections, according to Dr. R. D. Jeffs. He pointed out that effective treatment of the urinary infection may lead to disappearance of reflux in the child. Dr. Medovy said that with clearing of infection, local edema of the ureterovesical valve clears and the valve becomes efficient. Often reflux will be corrected spontaneously. Dr. Cameron stated that reflux is infrequently seen in adults, although, as emphasized by Dr. Campbell, reflux may be demonstrated in the adult by a voiding cystogram. When an I.V.P. and a retrograde pyelogram are normal in a patient with urinary infection, it is important to establish whether reflux exists or not and to treat it accordingly.

The revival of interest in quantitative studies of bacteriuria, including colony counts, has been largely stimulated by the work of Dr. E. H. Kass of Boston. Such counts, in order to be significant, require a very fresh specimen, trained personnel and time. Dr. Medovy and Dr. Jeffs said that they use colony counts very infrequently. Dr. Cameron said that at the Montreal General Hospital colony counts are used but that counts of 10^{10}/ml. of urine were used as the dividing line between contamination and true urinary infection as opposed to counts of 10^5/ml. of urine, as used by Kass. In discussing the significance of bacteriuria in pregnant women, Dr. Michael Kaye of the Montreal General Hospital reported that among 370 pregnant women with untreated bacteriuria, there was no increased incidence of premature delivery or of congenital anomalies. All of these women were private patients. Six weeks post partum, 75% of them had urinary colony counts of less than 10^5/ml. Dr. Medovy expressed the opinion that prematurity is more common in the lower economic class, and he further stressed the importance of Kass' work at the Boston City Hospital which showed an incidence of 6-7% prematurity in pregnant women with urinary tract infection. It remains to be proven by further controlled studies whether or not there is a cause-and-effect relationship between bacteriuria and premature delivery.

Treatment of urinary tract infection was discussed at some length. Dr. Jeffs distinguishes three groups of children with urinary infections on the basis of preliminary examinations. The first group has evidence of urinary tract obstruction, and surgical correction can be employed in treatment. The second group shows reflux, with or without residual urine, and is treated conservatively. The third group has no radiological abnormality to account for the infection. Dr. Medovy stated that he usually treats acute urinary tract infection in children according to age and symptomatology. In sepsis of the newborn infant, there is often asymptomatic urosepsis which requires urine culture and sensitivity to permit effective therapy. Patients from 1-2 years of age with urosepsis may not have urinary symptoms but may present with fever, convulsions and failure to thrive. A high index of suspicion of urosepsis on the part of the physician may lead to proper diagnosis. In older children, dysuria, pain and frequency often accompany acute urinary infection and require prompt investigation and treatment. Dr. Cameron expressed his support for the use of chloramphenicol as one of the most useful antibiotics for urinary infections, since it is concentrated about ten times in the urinary tract where it is bactericidal. With confirmation of bacterial sensitivity to chloramphenicol, Dr. Cameron stressed continued therapy with full doses for a period of time. Later, sulfonamides may be substituted and carried on two to three months, even if the urine is clear on culture and microscopic examinations. Others claim that treatment should be continued from several months to several years. Dr.

*See also page 271, issue of July 29.

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Cameron warned that the initial use of small doses of chloramphenicol may lead to bacterial resistance. It was acknowledged that such regimens might not be practical in office or home care of urinary tract infection, but the physician must always suspect pyelonephritis in a patient who presents with evidence of urinary tract infection. Undoubtedly many cases will clear up in ten days to three weeks of treatment. The physician must be certain, if short-term therapy is started on the assumption of a diagnosis of cystitis, that repeated urinalyses are performed in the following months.

Dr. Campbell then entered the controversy of drug therapy by stating that he never uses chloramphenicol first but initiates therapy of acute urinary infection with sulfonamides until culture and sensitivity studies indicate a need to change drugs. He further stressed that when tuberculous infection of the urinary tract is suspected, repeated cultures for acid-fast bacilli and tuberculin tests may help to confirm the diagnosis. A negative tuberculin test does not rule out tuberculosis but is strong evidence against it. One must suspect tuberculosis when confronted with a sterile urine containing pus cells. Dr. Medovy agreed with the use of sulfonamides initially and reserved the use of chloramphenicol when it is the drug of choice. He stressed that chloramphenicol should never be used routinely in the treatment of otitis and sore throats. Sulfonamides carry less risk than chloramphenicol. Dr. Cameron argued that the incidence of aplastic anemia with chloramphenicol is not clearly defined and pointed out that sulfonamides are not without risk, referring briefly to the occurrence of interstitial nephritis after the use of sulfonamides. He re-emphasized that in the treatment of acute urinary infection there should be a sense of urgency, since pyelonephritis is reasonably common and can become serious. An early bactericidal effect as achieved by chloramphenicol is important. The objective should be to treat the highest proportion of cases most effectively in the shortest period of time. Dr. Jeffs agreed with the use of chloramphenicol in urinary infections. He treats patients with acute urinary infections for three months initially, but if infection recurs after such a course, treatment is extended by the use of sulfonamides or nitrofurantoin (Furadantin) for longer periods. He explained that in order for methenamine mandelate (Mandeline) to be effective, urine acidification with a pH of less than 5.5 is required. This is difficult to achieve and maintain in a child. He concluded that it is possible to be giving long-term drug therapy without effect because of changing bacterial flora and thereby continuing infection. Therefore, regular urinalyses with repeated cultures are required in long-term administration of drugs for urinary infection.

Dr. Campbell commented on office treatment without the aid of radiological studies. He advised initial treatment with sulfonamides for a two-week period, re-examination, and follow-up for three months. If the infection is recurrent or chronic, a complete investigation and treatment for a prolonged period is indicated. Pus may be found in the urine in chronic pyelonephritis over many months, even when the patient is receiving appropriate medications. Dr. Cameron then added that those patients with unresponsive infections need special attention. In particular the physician must check for evidence of obstruction, which may have been overlooked. During long-term therapy it was felt to be advisable to perform urine cultures every two to four weeks in the acute period, for up to three months, in order to detect any changes in the bacterial flora.

In diabetics, urinary infection was said to be three to four times more common, but this has not been so in children, according to Dr. Medovy. Dr. Jeffs indicated that he had not seen a diabetic child with urinary infection in four years. Dr. Cameron agreed that, in adults, urinary infection is more common in diabetics. Treatment is the same as for non-diabetics, but it generally takes longer to eradicate the infection. Colony counts greater than 10^5/ml. were found in 11% of 104 diabetic males and in 27% of 137 diabetic females.

Dr. Medovy observed that hypertension in children is most commonly associated with aortic coarctation or acute glomerulonephritis. Few cases of pyelonephritis lead to hypertension in childhood, but pyelonephritis must be excluded as a possible cause. Dr. Cameron indicated that 25% of patients with malignant hypertension have concurrent pyelonephritis and that 50-60% of patients with pyelonephritis have hypertension. Usually the pyelonephritis is bilateral, but one sometimes encounters unilateral pyelonephritis, which may raise the question of nephrectomy in treatment. It is advisable to treat the hypertension with the usual antihypertensive agents, even though the hypertension is due to refractory pyelonephritis.

Dr. Jeffs stated that the procedure of urethral dilatation in children is probably justified only in the treatment of urethral narrowing by stricture. Dilatation should not be employed simply as an adjuvant measure to treat urinary infection.

Renal biopsy was felt to have only a limited place in the diagnosis of pyelonephritis. However, as pointed out by Dr. Cameron, renal biopsy may be helpful in chronic renal disease when no precise diagnosis is attainable by other means. Some Europeon authorities have suggested that culture of the biopsy specimen is possible, but this may be difficult. Similarly, only limited assistance is to be expected from culture of the blood on the biopsy needle.

J. W. IBBOTT

"DEAFNESS, ITS DIAGNOSIS AND MANAGEMENT"

Chairman: *Dr. Fernand Montreuil*, Montreal
Panelists: *Dr. W. Alexander*, Winnipeg
Dr. K. McAskile, Toronto
Dr. H. E. McHugh, Montreal
Dr. Paul Robert, Montreal

Hearing was defined by DR. W. ALEXANDER, Head, Department of Otolaryngology, Winnipeg General Hospital, and Chairman, Department of Otolaryngology, University of Manitoba, as the perceptual pattern of auditory sensation which results from auditory stimulation by sound energy. As such it depends not only upon an intact auditory system but also upon the sum total of the past experiences of the organism, and the ability of the organism to learn from them. This then becomes the basis of language and of communication in man.

Hearing loss may be either conductive or perceptive. Conductive deafness is a mechanical effect due to obstruction to conduction of sound energy to the sensory or inner ear. The obstruction may result from congenital atresia of the external canal, from obstruction of the external canal by foreign body or cerumen, from destruction of the tympanic membrane, from dissolution of continuity of the three ossicles of the middle ear,

from fixation of the stapes in otosclerosis, or from blockage of the Eustachian tube. Blockage of the Eustachian tube interferes with the movement of the ossicles and induces hearing loss. In adults this may result from tumour of the nasopharynx. In children the obstruction may be mechanical, due to enlargement of the adenoids, or it may be associated with allergic effects or the effects of recurrent upper respiratory infections of the lining mucosa. Evidence of fluid in the middle ear, or recurrent otitis, is an indication for removal of obstructing adenoids. Patients with conductive deafness will invariably speak quietly. They hear well in a noisy atmosphere where voices are raised to overcome the ambient noise level. To make these people hear, the responsible mechanical deformity must be overcome, or the intensity of the sound must be increased so that the sound energy is conducted to their sensory cells.

Perceptive nerve deafness results from changes in the end organ of hearing. Congenital deafness may be inherited or may result from erythroblastosis fetalis, from the administration to the mother of toxic agents which cross the placental barrier, or from virus infections *in utero*. In the adult, presbycusis, a progressive diminution in acuity with age, begins at about age 20, and is evident by age 40. Other causes of perceptive deafness include acoustic trauma (blast injury or persistent noise), toxic drugs, acoustic neuroma, cerebrovascular diseases and demyelinating diseases. This patient needs quietness in which to hear. He cannot hear at a cocktail party or over the telephone. He is liable to say "Don't shout at me."

Dr. P. Robert discussed those infectious diseases which cause deafness. In former years, cerebrospinal meningitis was a common cause, as was typhoid fever. Mumps and herpes zoster involving the eighth nerve rarely cause deafness. Those agents with a toxic effect on the eighth nerve include streptomycin, neomycin, kanamycin, quinine, aspirin and colchicine. Streptomycin affects the vestibular division of the eighth nerve. Dihydrostreptomycin damages the cochlear division of that nerve. Hearing loss is more serious than vestibular loss, so that streptomycin is the preferred therapeutic drug. Hearing losses due to streptomycin are irreversible, and may be delayed in appearance.

Early recognition of deafness in children is most important. Hearing loss is a form of sensory deprivation, a deprivation of one of the material resources from which the mind develops. Lack of one sensation alters the basis of perception and the development of experience. Dr. H. E. McHugh, Director of the Department of Otolaryngology, Montreal Children's Hospital, stated that if a child could not talk by 30 months, he was either deaf, brain injured, emotionally disturbed, or retarded. One must distinguish between these on the basis of the behaviour pattern of the child. Deafness can often be distinguished by the age of six months. Proper early diagnosis is of the utmost importance in the management of these children.

Otosclerosis is a common and treatable cause of deafness in the adult. The pathology of the disease, the progressive sclerosis of the bony edges of the oval window with ultimate fixation of the stapes, and involvement of the footplate by the process, was illustrated in detail by Dr. McHugh. Therapy consists in construction of a pathway to conduct sound waves by which the fixed stapes is bypassed. In 1948, Lambert developed the fenestration procedure, an operation in which an opening at the horizontal semicircular canal is created. In 1953, Rosen began mobilizing the stapes. This soon became refixed. The procedure used now is to remove the stapes, reconstruct the oval window, and put in a prosthesis to transmit sound energy from incus to oval window.

Acute noise-induced hearing loss was demonstrated. Recovery time was a large multiple of the time of exposure. The relationship of the acute noise-induced hearing loss to permanent loss is unknown, but Dr. Alexander felt that the principle of frequent breaks during which the person was completely removed from the noisy area should be used as a guide in industry.

C. A. GORESKY

Thursday, June 22

"EMERGENCIES IN THE NEWBORN"

Chairman: *Dr. H. Medovy*, Winnipeg
Panelists: *Dr. C. A. Stephens*, Toronto
Dr. R. H. Usher, Montreal
Dr. J. M. Bowman, Winnipeg

The members of the panel were introduced by the Chairman, DR. H. MEDOVY, Professor and Chairman, Department of Pediatrics, University of Manitoba, who went on to say that the panel would concentrate on certain conditions in the newborn period which were emergencies of a potentially remedial nature, and a group in which tremendous advances in treatment had been made.

The three panel members would deal with jaundice, bleeding and anemia; respiratory emergencies; and surgical emergencies, respectively. The form of the panel was to consist of answers by the panel members to specific questions asked by the Chairman.

Dr. J. M. Bowman, University of Manitoba, and Children's Hospital, Winnipeg, discussed questions pertaining to jaundice, anemia and bleeding in the newborn period. In the management of jaundice appearing in a baby under 24 hours of age, the point stressed was that such jaundice is abnormal, should always be investigated and is usually due to erythroblastosis. Indirect bilirubin, the cause of the jaundice, is toxic, and if allowed to reach levels greater than 20 mg. % may cause a type of brain damage called kernicterus. The risk of kernicterus rises to as high as 50% if the bilirubin level exceeds 30 mg. %. The Coombs test will be positive in all instances, except in ABO erythroblastosis, where major blood group incompatibility (mother O, baby A or B) is presumptive evidence and spherocytes in the baby's peripheral blood smear confirmatory evidence of ABO hemolytic disease. No matter what the type of erythroblastosis, exchange transfusion should be carried out whenever necessary to keep serum bilirubin levels below 20 mg. %. In the rare newborn with a negative Coombs' test and compatible group who is jaundiced within 24 hours of birth, anoxia at birth, sepsis, toxoplasmosis, cytomegalic inclusion disease and syphilis must be borne in mind as causes.

Prematurity plus erythroblastosis carries an even greater risk of kernicterus. In the premature weight range, 3½-4½ lb., exchange transfusion should be used to keep serum bilirubin levels below 18 mg. %, and in the premature under 3½ lb. every effort should be made to keep the serum bilirubin level below 17 mg. %.

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The non-erythroblastotic, hyperbilirubinemic premature is not at quite the same degree of risk, since in the erythroblast, circulating heme pigments, anemia and antibody-coated red cells interfere further with cellular oxidation. Nevertheless, since indirect bilirubin is toxic, a non-erythroblastotic premature infant whose indirect serum bilirubin level reaches or exceeds 20 mg. % in the first six to seven days of life, should undergo exchange transfusion. A puzzling factor is the great variability of incidence of non-hemolytic hyperbilirubinemia reported from different premature nurseries across the continent.

Physiologic jaundice is due to immaturity of the glucuronide conjugating mechanism in the newborn liver, which delays bilirubin excretion, and accounts for the development of visible jaundice in from 20 to 70% of all newborns in the second to fifth day of life. This physiologic jaundice is not related to blood group incompatibility and the question of treatment is controversial. Since again, indirect bilirubin is toxic, it might be just as well to exchange even a mature non-hemolytic infant, if the indirect serum bilirubin rises much above 20 mg. %. It must not be forgotten that anoxia and infection are potent aggravators of neonatal jaundice.

Normal cord hemoglobin values were stated to range from 14 to 19 g. %, with heel prick hemoglobins, shortly after birth, ranging from 15 to 22 g. %.

Anemia immediately at birth is most frequently due to erythroblastosis fetalis. Bleeding from ruptured fetal vessels during labour, fetal transfusion of the mother before birth, accidental incision of the placenta during Cesarean section and bleeding from one monozygotic twin into another (usually B into A) will cause severe anemia. A large cephalohematoma or bleeding into the aponeurosis of the scalp may cause later anemia.

Investigation of the anemic newborn consists initially in ruling out hemolytic disease by means of a Coombs' test of the baby's blood, by determining the mother-baby blood group relationships, and by searching for antibodies in the mother's serum and for spherocytes in the baby's blood. If jaundice is associated with the anemia, hemolytic disease is likely.

In investigating the possibility of bleeding before or during birth as a cause of anemia, a history of vaginal bleeding (particularly if the blood is fetal, as proved by NaOH test), torn cord or placental vessels noted on examination of placenta and membranes, cut placenta at Cesarean section and twin birth with the other twin plethoric, may be very helpful in making such a diagnosis. A reticulocytosis of greater than 10% or erythroblastosis of greater than 15% in the absence of hemolysis is strong evidence of fetal blood loss. The finding of significant numbers of fetal cells circulating in the mother's blood, utilizing a test devised by Dr. A. Zipursky of the University of Manitoba, is strong evidence that the anemia has been brought about by the fetus transfusing the mother before birth with large amounts of blood, a rare but well-documented occurrence.

Indications for transfusion in the newborn period, excluding erythroblastosis, are as follows: emergency transfusion for pallor and shock at birth with evidence of fetal bleeding; emergency transfusion for pallor and shock at birth with no evidence of bleeding but failure to respond to resuscitation; elective transfusion is probably indicated for a hemoglobin value below 10 g. % at birth, since this level of hemoglobin will inevitably drop much lower in the first six weeks of life. Such a transfusion may be quite safely delayed until the hemoglobin drops below 6 g. %. Usually, 10 c.c. of blood per lb. body weight is given; rarely more if the child is shocked with proved blood loss; frequently less (5 c.c. per lb.) if the anemia appears to be chronic owing to chronic blood loss and the venous pressure is elevated, as shown at catheterization of the umbilical vein. A partial exchange transfusion may actually be safer in the severely anemic newborn with an elevated venous pressure. All blood used for transfusion is grouped, except in grave emergencies when O Rh negative blood is given. Although ideally cross-matching should be carried out, Dr. Bowman said that he did not routinely do so, and added that he had never had reactions from unmatched blood (major group and Rh compatible) given to newborn infants.

In differentiating pallor of asphyxia from pallor due to fetal bleeding at birth, history is important. Difficult labour makes one think of asphyxia. Vaginal bleeding (if blood is proved to be fetal) makes one think of fetal bleeding. Response to resuscitation, if prompt, makes asphyxia most likely. If there is not a prompt response to resuscitation, the umbilical vein should be catheterized. If the venous pressure is negative to +1 or +2 cm., 5 c.c. of emergency blood per lb. of body weight should be transfused at once (quickly). Such a small rapid transfusion may save the baby who has bled, and will not harm the baby who is asphyxiated.

Bleeding in the newborn period may be due to: (1) severe hemolytic disease (the commonest cause); (2) anoxia and birth trauma; (3) local gastrointestinal lesions, such as fissures, polyps, Meckel's diverticulum and obstructive anomalies; (4) specific clotting defects, such as thrombocytopenia and the hemophilia group; (5) sepsis, and (6) so-called hemorrhagic disease of the newborn which, excluding hemolytic disease, is the commonest cause of bleeding at this age.

True fetal or infant bleeding may be differentiated from vomiting or passage of swallowed maternal blood by a simple test. Vomitus or stool containing red blood is mixed with tap water and filtered or centrifuged. One part 1% (¼ N) NaOH is mixed with 5 parts supernatant or filtrate. After two minutes a yellow colour denotes adult hemoglobin and the swallowed maternal blood syndrome; a pink colour, fetal hemoglobin and true bleeding. The same test may be used to determine whether vaginal bleeding prior to or during labour is fetal in origin.

Although vitamin K in large doses is toxic, particularly to the premature, causing hemolysis, kernicterus and death, doses less than 2.5 mg. are quite safe (vitamin K_1 is even safer). Since May 1960, 1 mg. vitamin K (Kavitan) has been given routinely at the Winnipeg General Hospital Women's Pavilion to all babies entering the newborn nursery. The incidence of hemorrhagic disease has dropped from 3.02 per thousand to 0.67 per thousand, and the incidence of bleeding severe enough to require transfusion has dropped from 1.15 to 0.22 per thousand.

Dr. R. Usher, Royal Victoria Hospital, Montreal, dealt with respiratory emergencies in the newborn period. In defining the respiratory distress syndrome, Dr. Usher stated that he considered this syndrome to be a distinct entity and not a catch-all for all babies with breathing difficulties. Three pathognomonic signs of the respiratory distress syndrome are: (1) indrawing or retraction of the chest wall with each inspiratory

effort, (2) grunty breathing, and (3) poor air entry when the chest is auscultated. Although tachypnea, cyanosis and rales are also usually present, they are not specific, and are often present in babies with other conditions.

The respiratory distress syndrome usually develops in prematures within the first three hours of life, and it is important that a physician familiar with this syndrome see and evaluate the premature (especially the infant under 4 lb.) in this all-important first three hours.

Other causes of breathing difficulties must be remembered. They are: pneumonia, congenital heart disease, fetal aspiration syndrome, aspiration due to tracheoesophageal fistula, diaphragmatic hernia, pneumothorax and pneumomediastinum. Pneumothorax and pneumomediastinum may be difficult to differentiate from the respiratory distress syndrome. In the full-term infant the diagnosis of respiratory distress syndrome should be made with caution, since difficult breathing in such infants is usually due to other causes (except in term babies of diabetic mothers or babies born by Cesarean section where the respiratory distress syndrome is common).

A chest radiograph taken of the baby with respiratory distress syndrome usually shows a reticulogranular type of diffuse opacity with widened mediastinum; and since air is present in the trachea and major bronchi, these show up as an air bronchogram. The radiograph is not diagnostic and is not of as much value as the already mentioned clinical signs in making the diagnosis of respiratory distress syndrome. The chief value of a radiograph is to rule out pneumothorax and diaphragmatic hernia, two emergencies where prompt diagnosis and surgical intervention may be life-saving.

Hyaline membrane disease is a postmortem diagnosis, the term originating with Farber and Wilson. Most babies with the respiratory distress syndrome who die, show massive pulmonary atelectasis and liver-like lungs; and most, but not all, have hyaline membranes lining bronchioles and alveolar ducts.

In outlining what a physician should do if he is called to see a baby with cyanotic spells, difficulty in breathing, or rapid respirations without actual difficulty in breathing, Dr. Usher stated that the above question leads into the differential diagnosis of respiratory problems in the newborn.

In the pale baby with laboured respirations, a drop in the hemoglobin value in the first hour or two of life (instead of the usual rise) makes one think of fetal bleeding. Severe cyanosis in a baby with very quiet or displaced heart sounds makes one think of pneumomediastinum or congenital diaphragmatic hernia. A radiograph is diagnostic in these cases. Treatment may have to be very prompt if a life is to be saved. In a premature infant, laboured breathing means the respiratory distress syndrome.

If there is a history of difficult labour and delivery at term, and an asphyxiated baby who resuscitates promptly and looks well for a few hours, then becomes ill with poor colour, tachypnea (respiratory rate 90-120) and coarse hyperventilatory breath sounds with some fine rales, one is probably dealing with the so-called fetal aspiration syndrome. Congenital heart disease must also be considered. Extremely rapid breathing and relatively good air entry help to differentiate these babies (who are usually term babies) from those with respiratory distress syndrome. Such differentiation is important, because the infant with the fetal aspiration syndrome usually goes into heart failure with enlarged heart and liver. Measures to control heart failure, such as digitalis, may be very helpful.

The respiratory distress syndrome is an important contributor to neonatal morbidity and mortality. One premature in seven develops the syndrome and half who develop it die. One term baby in 400 develops respiratory distress and one-fifth die. Half of the so-called term babies who develop respiratory distress are delivered by Cesarean section. Twenty-nine of 30 such infants studied recently were under 7 lb. and 38 weeks' gestation. Thus, although not classed as prematures, they were not full-term infants. Elective Cesarean section should be postponed until the mother is as near 40 weeks' gestation as possible. The respiratory distress syndrome is primarily a disease of prematurity and it causes 40-60% of all neonatal mortality.

There are many theories put forth as to the cause of respiratory distress syndrome. There are still no facts which bolster any of these theories. However, some facts are known. This is a disease that has begun at birth. There is no latent period. The cause is operating prior to the infant's first breath. The absence of a low surface tension layer, normally found lining pulmonary alveoli, has been postulated. At postmortem examination, lungs of babies dying of respiratory distress have low fibrinolytic activity. One theory is that pulmonary edema fluid deposits fibrin, which clots because of the low fibrinolytic activity of the lung and produces respiratory obstruction. Because the hyaline membrane found post mortem contains fibrin, the membrane is believed to be due to fluid transuding from pulmonary vessels into the lung. Others believe that aspiration of blood is a factor. None of these hypotheses have helped in the management of the mother to prevent the development of the syndrome or in the treatment of the baby once it has developed the syndrome. James believes that some factor *in utero* produces asphyxia in babies who after birth develop respiratory distress.

In managing the infant with respiratory distress, one must be aware that certain metabolic disturbances develop in this condition. Respiratory and metabolic acidosis develop within ½ to 1 hour of the onset of symptoms. Blood pH may be anywhere from 7.0 to 7.2. Tissue breakdown with release of potassium, nitrogen and phosphate occurs. Because of the poor renal function of the premature newborn infant, these materials build up in the baby (a serum potassium value of 7 to 13 mEq./l. and a blood urea nitrogen value of 60 to 80 mg. %). These babies auto-intoxicate themselves. The electrocardiogram shows bizarre hyperkalemic patterns. These metabolic events may be corrected or prevented by administration of 10% glucose intravenously, with varying amounts of sodium bicarbonate (5-15 mEq./100 c.c.) given at the rate of 30 c.c. per lb. per day. With very severe hyperkalemia, small amounts of insulin may be given. These measures prevent tissue breakdown, and acidosis, keep potassium levels normal, and have reduced the mortality rate in respiratory distress from 40% to 20%. At the Royal Victoria Hospital, Montreal, in 1960, premature mortality in the 500-2500 g. weight-group was 8% (in previous years, 14-20%). Thus, in this group, neonatal mortality would appear to have been halved.

Radiographs are not important in diagnosing respiratory distress. They are helpful in the infant over 4 lb. where other causes of respiratory distress, such as

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pneumothorax or diaphragmatic hernia, must always be considered. At a later stage of the syndrome, radiographs may be valuable, particularly if the infant with respiratory distress is doing poorly, since 5 to 10% of babies with respiratory distress develop pneumothorax and pneumomediastinum.

In the management of the infant with respiratory distress, the advantages of a large premature nursery with microchemistry laboratory facilities may not outweigh the risk of transferring a premature infant with respiratory distress. If the essential facilities, such as proper incubators, nursing staff and above all a physician trained in premature intravenous techniques and experienced in the management of such infants, are available, transfer to a larger centre is not indicated. The important advance in the treatment of prematures with respiratory distress is early continuous intravenous glucose and bicarbonate. This may be administered in any hospital nursery where scalp vein techniques are familiar procedures, provided there is a dedicated physician or resident who will keep the intravenous running.

Dr. C. A. Stephens, Hospital for Sick Children, Toronto, and Associate in Surgery, University of Toronto, opened his discussion of surgical emergencies in the newborn period by stating that although the number of such emergencies in a year, in any one pediatrician's practice, is not great, prompt recognition when one appears is essential if good results are to be obtained by surgical intervention.

Congenital diaphragmatic hernia, when encountered, may require the most urgent surgical treatment. Eighty per cent are on the left side, with the intestine, colon, spleen and possibly the stomach passing into the pleural space. Expansion of the left lung is prevented, and the right lung is compressed by the shifted mediastinum. The infant, often cyanosed and usually distressed immediately at birth, becomes worse as swallowed air distends the gut, further compressing the lungs. Usual symptoms are increasing cyanosis, dyspnea, tachypnea and tachycardia. On examination the involved side, usually the left, has diminished or absent breath sounds and may be tympanitic to percussion. Bowel sounds may be heard in the chest. The heart will be heard on the right (when the hernia is on the left). The abdomen appears unusually scaphoid. Once suspected, the diagnosis is easily confirmed by radiography. Once diagnosed, immediate surgical repair is essential. The stomach and intestinal tract should be kept decompressed by suction through a duodenal tube. Endotracheal intubation and intermittent positive pressure oxygen may be necessary to keep the child oxygenated prior to operation. Usually the hernia is repaired transabdominally with closure of the diaphragmatic defect. The postoperative course may be stormy, recovery depending upon the ability of the ipsilateral lung to expand once the hernia is repaired. Contralateral pneumothorax postoperatively is not infrequent, and must be watched for in any postoperative patient with diaphragmatic hernia who develops respiratory distress. Vigorous attempts to expand the ipsilateral lung by positive pressure, at the time of operation, should be avoided, because of the possibility of causing pneumothorax. Initial symptoms vary in severity. In those babies whose symptoms are so severe that diagnosis and treatment have to be undertaken in the first 24 hours of life, the mortality is 50%. In all other such infants, the mortality is about 10%.

Esophageal atresia, with or without associated tracheoesophageal fistula, is one of the most common major surgical emergencies in the newborn period. In the preceding 10 years, 201 children with the above lesion were admitted to the Hospital for Sick Children, Toronto, compared to 122 admitted with all other congenital atresias of the alimentary canal, excluding imperforate anus. Eighty-five per cent had atresia of the upper end of the esophagus, with a fistula leading from the trachea into the lower end of the esophagus. Presenting signs are drooling of saliva, choking, cyanosis and inability to swallow. Aspiration occurs when secretions fill the upper pouch and spill into the trachea, or when gastric contents are regurgitated into the distal esophagus and then through the fistula into the trachea. This second form of aspiration leads to widespread pneumonitis owing to the irritating effects of gastric juice. Diagnosis is made by attempting to pass a rubber tube into the stomach (the rubber should not be too soft). If an obstruction is encountered, instillation of 1 to 2 c.c. of Lipiodol via the catheter, followed by radiographic examination, will outline the lesion.

Early diagnosis and treatment, before aspiration has produced widespread pneumonia, is essential for good surgical results. Preoperatively, these infants are nursed semi-upright to lessen gastric aspiration, the upper pouch being kept empty by continuous or intermittent suction. All of these patients should be given antibiotics for their incipient pneumonia.

Division of the fistula and primary esophageal anastomosis is the surgical treatment of choice. Rarely, when the gap between the two esophageal segments is very great, cervical esophagostomy and gastrostomy with ligation of the fistula may be the only procedure which can be done, followed at a later date by esophageal reconstruction, using colon or small intestine. Expert, intensive postoperative care is essential. Frequent pharyngeal suction and care to prevent overhydration are important. Some patients will require feeding gastrostomy and some will develop anastomotic strictures requiring dilatation. At present, those children diagnosed early, before pneumonia develops, who are without associated anomalies and over 5 lb. at birth have a 70 to 80% chance of survival. The mortality if diagnosis is delayed, if there are associated anomalies, or if the baby is small and premature, remains very high.

Neonatal intestinal obstruction may be divided into two groups, high and low. High obstruction may not be diagnosed early, because distension is not a feature, and in some cases bile may be absent from the vomitus. Common causes of high obstruction are duodenal atresia and stenosis, malrotation of the colon (with or without volvulus), annular pancreas, jejunal atresia or stenosis. Early vomiting is the common feature. Bile is usually, but not always, present and abdominal distension is absent. Since vomiting is frequent in the newborn, the possibility of obstruction may not be entertained for some time. A radiograph of the abdomen is usually diagnostic, and once the condition is diagnosed prompt operative intervention is necessary. The type of procedure to be carried out depends on the type of lesion encountered. In duodenal obstruction, from whatever cause, the so-called double bubble,

gas-distended stomach and duodenum seen on a radiograph is diagnostic.

Malrotation of the intestine may cause high obstruction for two reasons. First, a peritoneal band may pass from the cecum across the duodenum, obstructing it. Secondly, volvulus of the small intestine may be present. If volvulus is present, the blood supply to the intestine may be impaired, and an emergency of the first order is present. If the patient is not operated upon at once, gangrene of the intestine will develop, with its attendant 100% mortality. Volvulus should be suspected in a baby who has been vomiting and looks shocked with signs of peritonitis (tense, tender abdomen with absent bowel sounds and respiratory difficulty). Blood may be present in the stools. Immediate operation is imperative. At present, 10% of infants with volvulus have small-bowel gangrene by the time they are diagnosed and operated upon.

In low intestinal obstruction, abdominal distension develops early in life. Vomiting, the vomitus always containing bile, is present. Absent or abnormal meconium is noted. Common causes are imperforate anus, congenital megacolon, ileal atresia or stenosis, meconium ileus, meconium plug and atresia of the colon.

Surgical intervention is not necessary in all types of lower obstruction. To determine whether large or small bowel is involved and the exact level of obstruction, a barium enema examination is necessary. In small bowel obstruction a microcolon is present, and one knows that ileal atresia or stenosis, meconium ileus or congenital megacolon involving the whole colon (very rare) is present. Laparotomy alone will decide which is present and the proper surgical treatment.

If barium enema examination reveals a narrow colon of variable length, then grossly dilated proximal colon, one is dealing with either congenital megacolon or the meconium plug syndrome. In the meconium plug syndrome the diagnostic enema may allow the evacuation of the plug and effect a cure. Repeated enemas may be necessary. In true congenital megacolon, the infant will continue to have obstruction, despite enemas, with recurring or persistent abdominal distension and vomiting. A narrow distal segment in association with these symptoms is diagnostic of congenital megacolon (Hirschsprung's disease). Occasionally, a rectal biopsy to demonstrate absence of ganglion cells may be necessary to establish the diagnosis.

Immediate treatment for congenital megacolon is performance of a defunctioning colostomy, definitive surgery being done later.

Imperforate anus is usually diagnosed on inspection, treatment depending upon how close the rectal pouch is to the perineal skin. In girls, if a rectovaginal fistula is present, simple dilatation with surgery at a later date is usually all that is necessary. In males, if the gap is small, a simple anoplasty may suffice. If the pouch is more than 1 cm. from the skin, a preliminary colostomy with deferred definitive surgery or a primary abdominoperineal pull-through is indicated.

In all lower intestinal congenital anomalies, there is a high incidence of associated urinary tract anomalies. Urological investigation is warranted in all infants presenting with low intestinal obstruction.

Dr. Stephens closed by saying that because of the complexity of the lesions which cause surgical emergencies in the newborn and the necessity for special nursing and postoperative care, such infants should be transferred to large, well-equipped centres where there are experienced pediatric surgeons, residents and nursing staff.

J. M. BOWMAN

"NEW CONCEPTS OF INFECTIOUS DISEASES OF CHILDHOOD"

Chairman: *Dr. Jules Charbonneau*, Montreal
Panelists: *Dr. A. R. Foley*, Quebec
Dr. V. Marchessault, Montreal
Dr. V. Pavilanis, Montreal
Dr. C. S. Anglin, Toronto

DR. J. H. CHARBONNEAU, Professor of Pediatrics, University of Montreal, after introducing the panel members, stated that in the past 20 years advances in the prevention and treatment of infectious diseases have completely changed the patterns of current infections. Old enemies, such as diphtheria and scarlet fever, are no longer feared. The staphylococcus is still a menace, as are many viral infections. The panel undertook to discuss limited but important aspects of viral and bacterial infection where recent advances have been made.

Dr. A. R. Foley, Provincial Epidemiologist, Quebec, discussed the general field of virus disease. He noted that there were some 50 viral diseases of man caused by 150 viruses of serologically distinct types, which could be divided into three classes: (1) respiratory, (2) enteric and (3) arthropod-borne.

The respiratory viruses include smallpox, chicken pox, measles, mumps, mononucleosis, primary atypical pneumonia, German measles, psittacosis, trachoma and yellow fever. Others less well classified in this group are the adenoviruses (24 types), the aseptic meningitis viruses (8 types), the viral encephalitis group, the common cold virus, the influenza viruses, the myxoviruses (6 types), and the hepatitis and herpes simplex viruses.

The enteroviruses consist of three families: (a) the three different polioviruses; (b) the Coxsackie group—A (24 types) and B (6 types); and (c) the ECHO viruses (25 strains).

Arthropod-borne viruses cause predominantly encephalitis and febrile illnesses. The Western encephalomyelitis virus is the only member of this group of significance in Canada.

Predominating poliovirus types vary from epidemic to epidemic. In the 1959 Quebec epidemic, Type I was the common strain isolated, to be replaced by Type III in 1960. As is well known, the severity of clinical poliomyelitis may vary from a simple febrile illness to fatal severe paralysis.

Coxsackie A viruses cause herpangina, aseptic meningitis, infantile diarrhea, lymphadenitis, and pericarditis, while the B group cause pleurodynia (Bornholm disease), aseptic meningitis, mild respiratory illness, pericarditis, orchitis, encephalomyocarditis in children, and rarely paralytic disease.

ECHO viruses may cause aseptic meningitis, febrile exanthems, infantile diarrhea and upper respiratory infections. The ECHO virus has caused paralytic illness in at least one instance.

Dr. Foley stressed that recovery is usual in viral infections. Serious sequelae occur only in three groups (particularly poliomyelitis), and only one, rabies, is universally fatal. The process of recovery from viral disease is not exactly similar to recovery from bacterial infection. It is more complex. Viral multi-

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plication is intracellular and involves disintegration of the original virus particle and the synthesis of new virus particles, utilizing host intracellular protein and nucleic acid. Antibody production in viral disease is not the only factor in recovery, since patients with agammaglobulinemia handle most viral infections very well. Once viral disease is established, administration of immune antisera does not affect its course. However, after recovery from viral infection, antibody is demonstrable and second attacks are rare. These phenomena are probably due to the intracellular multiplication of virus and the inability of antibody to get into the cell. Also, pure virus nucleic acid is infectious, and in this chemical stage it is unaffected by antibody. Environmental factors, such as temperature and pH, affect the multiplication rate and virulence of the virus. Non-antibody virus inhibitory substances, called interferons, are produced by the cells, and stop the cell-to-cell spread of virus. Once a cell has been infected by virus it cannot be reinfected by the same virus. As virus multiplication occurs, eventually the host cells may produce avirulent viral particles no longer harmful to man.

The above factors in man's defence against virus infections have only recently undergone exploration, and undoubtedly other factors still quite unknown are of importance.

Dr. V. Marchessault, of the University of Montreal, discussed the present status of measles immunization. He traced the history of attempts at measles immunization, beginning with Home in 1749, who used the variolation principle and again with Hektoen in 1905, using the same method. Unfortunately the measles produced was not attenuated.

A successful vaccine had to await the development of a successful medium for growing the virus. This was successfully carried out in 1938 by Platz, who, after producing measles in a monkey, passaged the virus 10 times through tissue culture cells of a 10-day-old chick embryo.

Initial vaccines produced in Philadelphia in 1939-1943 from virus grown on chorioallantoic membrane produced modified measles, which unfortunately did not offer protection against clinical measles.

In 1954, Enders and Peebles grew measles virus in tissue culture, obtaining the virus from blood and throat secretions of patients at the onset of the disease. The virus was passaged 24 times through human kidney cell culture and then passaged 28 times in primary human amnion cell culture. This same strain (Edmunston strain) was then successfully grown in chick embryo cell culture. The chick embryo adaptation reduced the virulence of the virus for monkeys, the virus producing very little fever or rash, even when injected intracerebrally. Nevertheless, 4-5 weeks later anti-measles antibody was present in high titre, and the monkeys were not susceptible to virulent measles.

Susceptible children were then given the same attenuated virus vaccine. Of 171 susceptible children inoculated, 96.5% developed neutralizing antibodies. The route of administration was important. Only a few children not immunized parenterally produced antibodies, and these received the vaccine intranasally. In the intranasal group who developed antibodies, the incubation period was longer, and the clinical reaction was not so severe as in the parenterally inoculated group, 83% of whom had febrile reactions and 48% rash, but always less severe than the usual clinical disease. None of the vaccinated children later developed clinical measles, during a period when many unvaccinated susceptibles came down with the disease. No measles could be traced in susceptibles from contact with a vaccinated individual during the clinical stage of his attenuated disease, and no virus could be isolated from 31 vaccinated children, blood and throat secretions being cultured at suitable intervals. Thus, live attenuated measles virus vaccine appears to be safe and effective.

Dr. Marchessault concluded by saying that this year we may have seen our last severe epidemic of measles, provided that the febrile reactions still present with the various measles vaccines can be mastered rapidly.

Dr. V. Pavilanis, of the University of Montreal, discussed the present status of poliomyelitis vaccination. Oral live attenuated poliomyelitis vaccines, although not widely used in Canada, are being used elsewhere with success. Live poliovirus vaccine was first used in 1950, antedating the Salk killed-virus vaccine.

There are still problems in the use of the formalized killed-virus vaccines, particularly regarding the number of initial injections necessary and the length and degree of immunity produced.

Studies in Canada in 1959 showed that after three or more doses of Salk vaccine, 87% in the 0-4 year age-group, 97% in the 5-19 year age-group and 74% in the 20-39 year age-group were protected, giving an overall protection figure of 95%. One injection produced some immunity in 45%, two injections in 80%, and three injections in 90% of individuals. A fourth injection raised the figure of protection to 95% in those injected. Vaccines may differ somewhat in their antigenicity. Also, vaccination under 6 months of age produces less protection, possibly because of the presence of passive antibody. The present suggested immunization schedule, if the individual is over 6 months of age, is two injections one month apart, followed by a third seven months after the second, and a fourth injection one year after the third. When the vaccine is combined with the standard diphtheria-pertussis-tetanus vaccine and immunization started at 3 months of age, it is suggested that three injections be given one month apart, followed by a fourth, seven months after the third, and a fifth injection one year after the fourth. If a child who produces antibodies to the Salk vaccine still has these antibodies at the end of one year, they persist for at least six years. Thus, immunity produced by the killed vaccine is quite long. Salk feels that even if measurable antibody disappears, if it was once present, exposure to poliovirus infection will cause rapid antibody response during the incubation period and protect the child.

Live poliovirus vaccine has been developed using strains of the three types which are least pathogenic to monkeys (i.e. will not produce paralytic disease in the monkey when inoculated intracerebrally). This oral attenuated vaccine has been widely used. Eighty million Russians and 18 million in the satellite countries have been given live virus vaccine. In the United States, the Sabin live strain has been used to vaccinate 300,000 children. In Canada, live attenuated virus has been used in Montreal and Quebec, Prince Albert and Wedgeport, Nova Scotia. Exact dosage and method of administration in Canada are still being worked out. In Prince Albert, the three strains were given together,

whereas in Wedgeport the three were given separately. Which method gives the best and most durable protection is not known.

A comparison of the effectiveness of Salk killed vaccine and Sabin live vaccine (in a very small group) showed that they are about equally effective (10% failed to develop antibodies in each group). The titre after administration of the Sabin live-virus vaccine was slightly lower. Two children who failed to develop antibodies to Sabin live virus were excretors of large amounts of adenovirus. Thus, competition by other viruses may prevent successful live poliovirus vaccination. Also, factors such as gastric acidity may prevent successful live virus vaccination.

Dr. Pavilanis concluded by saying that there are still some pitfalls in the universal application of live poliovirus vaccine, and the future may show that a combination of killed and oral live vaccines may ultimately provide the greatest protection against poliomyelitis.

Dr. C. S. Anglin, Hospital for Sick Children, Toronto, discussed the changing picture in our understanding of purulent meningitis in children. Bacteria still cause serious illness, especially in children. Despite all of the advances in nutrition, immunization, etc., the incidence and severity of bacterial meningitis has remained about the same. However, with our present antibiotic armamentarium, treatment and prognosis in purulent meningitis have been completely altered, making immediate and accurate diagnosis of great importance, so that proper therapy can be instituted.

The prognosis for patients under 2 years of age with meningitis remains poor, because signs and symptoms are vague, and diagnosis is often delayed. Stiff neck may be entirely absent in this group. The onset of meningitis frequently follows an upper respiratory infection. Early signs are irritability, a high-pitched cry, listlessness, resentment of handling, anorexia, vomiting, bulging fontanelle, seizures and rash (in meningococcal meningitis). In the older child, stiff neck and Kernig's sign are usually present. A lumbar puncture should be performed on the slightest suspicion.

In the newborn infant, signs of meningitis are even more vague. Umbilical infection or regurgitation and general failure to do well may be the only early signs of meningitis. A bulging fontanelle may not be present until later. There may be no fever. Poor colour and twitching should always make one suspicious. Immediate performance of a lumbar puncture in any newborn not doing well is our only hope of improving the still very poor prognosis in neonatal meningitis.

The etiologic agents in purulent meningitis of the newborn are usually *E. coli* and the Staphylococcus, whereas in the older infant and child *Hemophilus influenza B*, the Pneumococcus and the Meningococcus are the commonest organisms. At the present time in many patients with purulent meningitis the spinal fluid is sterile, as a result of widespread use of antibiotic therapy for upper respiratory infections. The possibility of meningitis must always be remembered in a child with an upper respiratory infection who is not doing well.

Purulent meningitis can be differentiated from tuberculous meningitis by the longer period of onset, the positive Mantoux test, the greater likelihood of a lung lesion, a lower spinal fluid cell count (mostly lymphocytes), and a pellicle, often with organisms, in the latter. Children with aseptic meningitis (due to mumps, Coxsackie, poliomyelitis, etc.) are usually not as sick, and the spinal fluid cell count is lower and, except initially, consists predominantly of lymphocytes. The spinal fluid sugar value is normal and the spinal fluid is sterile. Viral studies serve to make a retrospective diagnosis. Children with brain tumours, lead poisoning, etc., should be readily differentiated from children with purulent meningitis.

Before specific antibiotics were available, mortality from the purulent meningitides was extremely high (almost 100% in the pre-sulfa-antisera era). The mortality at the present time should be under 10%. General measures such as bed rest, intravenous fluids, sedation (sodium phenobarbital and paraldehyde) and oxygen, if necessary, are important. The spinal fluid should be examined by smear, Gram-stain and culture. The cell count, protein, sugar and chloride values should be estimated. A specific diagnosis should be possible from the spinal fluid smear examination in nearly 80% of cases within one hour of admission to hospital.

Specific treatment for infection with *Hemophilus influenzae B* (and also *E. coli*) consists in administration of chloramphenicol, 40 mg. per lb. per day given intramuscularly or intravenously 12-hourly. Neonates should receive half this dosage; prematures one-quarter this dosage.

Sulfadiazine or sulfisoxazole (Gantrisin) is also given, in a dosage of 2-3 grains per lb., intravenously, per day. Each medication should be given for seven days if the patient's course is satisfactory. The sulfonamide should be changed to an oral preparation as soon as possible.

Infection due to the Meningococcus is treated by administration of sulfadiazine or sulfisoxazole (Gantrisin), 2-3 grains per lb. per day, given intravenously initially.

Crystalline penicillin 500,000 units, intravenously or intramuscularly, should be administered every six hours. Treatment should be continued for five to seven days.

Fulminating meningococcemia, the so-called Waterhouse-Friderichsen syndrome, a medical emergency, may well be fatal no matter what the therapy used. Norepinephrine (Levophed) should be given by continuous drip, enough to maintain blood pressure. Use of steroids is controversial, since these individuals may already have high circulating steroid levels. Nevertheless, hydrocortisone (Solucortef) administered intravenously in high doses is advised. Oxygen should be administered. Aqueous adrenocortical extract is of doubtful value. Intravenous penicillin and sulfisoxazole should be given for seven days.

Meningitis due to the Pneumococcus is treated by administration of penicillin intravenously in massive doses, 2-3 million units every two to four hours. For the severely ill child, Dr. Anglin advises intrathecal penicillin, 5000 to 10,000 units diluted and given slowly. Sulfisoxazole may also be used. Treatment should be given for at least 10 days. In pneumococcal meningitis, particularly if recurrent, mastoid infection, sinus infection, dermoid sinuses, and hypogammaglobulinemia should be ruled out. Intrathecal steroids may

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prevent a spinal fluid pathway block if very thick purulent spinal fluid is present.

In the case of purulent meningitis where no organism is isolated, a combination of penicillin, sulfonamide and chloramphenicol should be used for 7 to 10 days.

Dr. Anglin quoted the results achieved in the treatment of purulent meningitis at the Hospital for Sick Children, Toronto, over an eight-year period. In *H. influenzae B* meningitis (199 patients), mortality was 8-12% and 5-15% had sequelae; in meningococcal meningitis (178 patients), mortality was 10% and 3-7% had sequelae; in Waterhouse-Friderichsen syndrome (24 patients), mortality was 62.5%; in pneumococcal meningitis (75 patients), mortality was 10-27% and 11-27% had sequelae; in meningitis due to unknown organism (77 patients, over a four-year period), mortality was 2.6% and 3.9% had sequelae.

Subdural effusions of fluid complicating meningitis, particularly in pneumococcal and hemophilus types, must be considered if fever persists or seizures or localized neurological signs develop. Subdural taps for diagnosis and treatment should be carried out, if this lesion is suspected.

Dr. Anglin concluded by stating that steady progress has been made in reducing the mortality and morbidity from purulent meningitis in childhood, but results in the very young are still not good. Physicians must always be on the alert to the possibility of meningitis, since only by early diagnosis will the mortality and morbidity rate associated with this disease improve.

The panel replied to several questions from the audience. Dr. Marchessault stated that the length of immunity after measles vaccination should be lifelong but that there is no proof of this. The only foreign antigenic material present in measles vaccine is a very small amount of egg protein. The dosage of measles vaccine is not critical, since an attenuated infection is produced and the virus multiplies in the body. Measles antibody takes about 10 days to develop following vaccination. A measles contact, if vaccinated the day of the contact, may be protected against virulent measles. He felt that killed-measles-virus vaccine is quite feasible; one disadvantage would be the multiple injections necessary. Measles virus vaccine is not effective during the first six months of life, if passive immunity is present. Children who have had measles do not show a rise in antibody if vaccinated with the attenuated vaccine.

Dr. Pavilanis stated that the incidence of asymptomatic poliovirus excretors should be less after use of Sabin live-virus vaccination than after Salk dead-virus vaccination. Children immunized with Sabin vaccine have been made poliovirus carriers, but this carrier state is shorter than in non-immune or Salk-vaccinated individuals.

Replying to other questions, Dr. Anglin said that enzymes, such as steptokinase-streptodornase, may be used in trying to break down spinal fluid block in purulent meningitis. However, they produce toxic effects and are probably not as good as steroids. Use of pancreatic desoxyribonuclease has produced inconsistent results.

"DYSMENORRHEA"

Co-Chairmen: *Dr. G. B. Maughan*, Montreal
Dr. Pierre Meunier, Montreal
Panelists: *Dr. Elinor F. E. Black*, Winnipeg
Dr. P. Dumas, Montreal
Dr. J. S. Henry, Jr., Montreal
Dr. E. H. Shabanah, Montreal

Three short papers were first presented, as a background to a question-and-answer period. The first paper was by DR. E. H. SHABANAH, Montreal, who described the results of his studies on the innervation of the uterus. Histological studies had been carried out on the pregnant bitch uterus. This recent work has now demonstrated clearly a parasympathetic supply to the uterus. Electrical stimulation of the parasympathetic fibres leads to contraction of the uterine musculature. It was felt that these findings are translatable to dysmenorrhea in the human.

The second paper was presented by Dr. J. S. Henry, Jr., Royal Victoria Hospital, Montreal. He stated that measurement of intramyometrial uterine pressure during the first half of the menstrual cycle reveals the presence of irregular, small contraction waves which occur every 30 to 60 seconds. These are known as "A" waves; their production is dependent on estrogen secretion. At mid-cycle, longer and more prolonged waves occur, every two to three seconds. These are known as "B" waves and their occurrence is dominated by estrogen and progesterone secretion. These two waves eventually merge. In an anovulatory cycle, in which there is no corpus luteum or progesterone secreted, only "A" waves occur and there is no pain when menstruation occurs. Dysmenorrhea is associated with hypercontractility or incoordinated activity of the uterine musculature or a combination of both. Contractions exerting a pressure as great as 330 mm. Hg have been measured during dysmenorrhea (in labour, contractions seldom exceed 100 mm. Hg). Pain occurs when the pressure exceeds the arterial system blood pressure of 125 mm. Hg. Oscillations due to the fluctuating pressure of the arterial tree can be seen on the intramyometrial pressure recording. These cease when the intramyometrial pressure exceeds 120 mm. Hg. Ischemia therefore is thought to be the cause of the pain of dysmenorrhea. The cause of the hypercontractility is the high degree of responsiveness of the uterine muscle to the influence of the estrogen-progesterone combination. The cause of the incoordinated activity is thought to be related to noradrenaline secretion.

The third paper was given by Dr. P. Meunier, Chief, Department of Gynecology, Hôtel-Dieu de Montréal, and Associate Professor of Gynecology, University of Montreal, who outlined in considerable detail the causes of dysmenorrhea, under the headings: organic, functional and mixed.

In reply to a question concerning the diagnosis of dysmenorrhea, Dr. Elinor F. E. Black, Professor and Chairman, Department of Obstetrics and Gynecology, University of Manitoba, and Chief of Obstetrics and Gynecology, Winnipeg General Hospital, stated that when a patient with dysmenorrhea had normal pelvic findings and a history which was not too helpful, her procedure was to try to determine the relation of the pain to the onset of the menses, how long the pain lasted, and how severe it was. In regard to the latter point, if it was learned that an aspirin gave satisfactory

relief, it could be presumed that the patient had a low pain threshold; at the other extreme, if the patient was in the habit of fainting, the pain could be judged to be severe.

Dr. P. Dumas, University of Montreal, expressed the opinion that women think menses should be painful and that this is a major contributing cause in dysmenorrhea.

Dr. Elinor Black stated that obstruction of the internal os of the cervix owing to fibrosis is infrequent and is due to conization or injudicious electrocauterization. A primarily tight internal os is a congenital rather than an acquired condition.

Dr. Meunier, when asked what he considered to be the mechanism of pain in endometriosis that gives rise to dysmenorrhea, said that the concomitant pronounced inflammatory reaction explained this.

All of the participants seemed to be agreed that treatment of endometriosis by administration of 200-250 mg. per month of male hormone was a satisfactory form of therapy. This dosage did not produce masculinization; this was thought to be accounted for by the high output of estrogens in such patients. However, it was also agreed that most of these patients would, in the long run, have to undergo surgery. Since many will have become pregnant in the meantime (while taking male hormone), enabling the patient to have a baby or two before undergoing surgery justified this approach. As well, the pregnant state would have a therapeutic effect on the endometriosis.

Dr. Elinor Black added that she found fluoxymesterone particularly useful in the treatment of patients with endometriosis.

On being asked whether retroversion of the uterus was a cause of dysmenorrhea, Dr. Meunier expressed doubt that it was a direct cause, but felt that it could have an aggravating role.

A stem pessary in the treatment of functional dysmenorrhea was considered to be outmoded and not to be used. In some patients relief may be obtained for a month or two, but this could very well be a psychological effect.

In treating primary dysmenorrhea, Dr. Elinor Black said that she was in the habit of asking the girl the type of work she did (whether standing or sitting most of the day) and whether she had a boy friend. Such a history could account for the presence of chronic pelvic congestion. Self-help in the form of knee-chest exercises would then be advised. In a second type the patient would be anemic, worn out and nervous, invariably with a mother who pushed her into many activities. This debilitated patient should receive appropriate treatment, including the recommendation to cut down on the number of activities engaged in, and treatment of the mother. In a third group who do not fit into one of the above two, the phenylbutazone derivative, oxyphenbutazone (Tandearil), was found by Dr. Black to be a highly satisfactory drug in this condition, given as one tablet three times daily on the two days before and on the first day of the menstrual period.

Dr. Shabanah was optimistic that an appropriate autonomic nervous system drug would be developed, with minimal side effects, that would offer relatively specific therapy for dysmenorrhea.

Dr. Henry concluded the session. He stated that when treating primary dysmenorrhea, removal of other additional stresses was of great importance. He pointed out that frequently the woman with primary dysmenorrhea has premenstrual tension and that it is to be expected that she will be more sensitive to pain when her period follows upon this bodily state. He recommended that attention also be directed to treating the premenstrual state by a low-salt diet, diuretic and sedative, as an aid in the treatment of primary dysmenorrhea.

"RADIATION PROTECTION IN DIAGNOSTIC RADIOLOGY AND IN INDUSTRY"

Chairman: *Dr. D. L. McRae*, Montreal
Panelists: *Dr. R. C. Burr*, Kingston
Dr. A. Jutras, Montreal
Dr. F. D. Sowby, Ottawa
Dr. C. G. Stewart, Chalk River

DR. R. C. BURR, Professor of Radiology, Queen's University, Kingston, Ontario, opened the session with a review of current knowledge of the hazards of ionizing radiation and a discussion of practical measures of radiation protection of patients subjected to diagnostic radiological procedures. Concerning the risk of genetic damage, he cautioned against the extrapolation of data obtained in mouse experiments, to humans. Although there remains a great deal to be learned with regard to the genetic effects of such radiation upon humans, it is a generally sound principle to employ common-sense measures to restrict human radiation exposure to the lowest possible degree, to minimize the risk of genetic damage. With regard to the leukemogenic potential of ionizing radiation, Dr. Burr pointed out that this form of energy is but one of several possible factors that may be involved in the widespread increase in leukemia incidence that is being recorded in many areas of the world. He commented on the results of one recent survey in which it was reported that radiologists showed an increased incidence of carcinoma of the skin and pancreas, as compared to that of non-radiologist physicians. There was, however, no appreciable difference in leukemia incidence between the two groups of physicians in this particular study. In essence, it seems to be the physician's duty to decide in each individual instance in which this problem arises, whether the relatively slight risk of diagnostic radiation is greater than that of omitting this potentially valuable diagnostic procedure. There is, however, no doubt that the dose of radiation to which the patient is exposed by such measures should be reduced to a minimum compatible with the production of a technically satisfactory radiograph, and that any unnecessary exposure should be scrupulously avoided. Particular care should be taken to guard against any accidental radiation of the gonads and to ensure that children and pregnant women receive no unnecessary exposure under any circumstances. Dr. Burr enlarged upon the technical aspects involved in protection of both patients and technicians during common radiological procedures, including those factors concerned with dosage and filtration, the target-skin distance, x-ray equipment and its shielding to minimize scatter radiation, proper shielding of fluoroscopic screens, the use of adequately protected gloves and aprons, the importance of preventing the x-ray beam from falling anywhere except on the screen, and proper dark-adaptation of the fluoroscopist's eyes for

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at least 10 minutes before screening. He advised against the practice of attempting to make multiple x-ray examinations of several patients in different rooms in quick succession. He also condemned the use of hand fluoroscopes. He noted that fluoroscopy of the chest delivers a greater radiation dose to the gonads than the routine chest radiograph procedure. The use of image intensifier devices helps to reduce the dose received by the gonads. Equipment should be checked periodically to ensure that it is accurately calibrated at all times and that there is no leakage about the cone. Radiological equipment in any setting should be monitored by various devices both within and adjacent to the room where radiological procedures are being conducted.

Dr. A. Jutras, Professor of Radiology, University of Montreal, discussed the protection of radiologists and technicians in the execution of diagnostic radiological procedures. To illustrate the significance of this subject, he pointed out that 75% of man-made radiations are used for diagnostic purposes. Professor Jutras then gave a most interesting account of the procedures that have been in progress in his department to develop the principle of image amplification and to adapt it toward the automation of diagnostic radiological procedures. He predicted that, in time, newer techniques would be perfected that would permit diagnostic radiology to be conducted completely by remote-control principles, thereby further minimizing radiation exposure of patients, radiologists and technicians alike, and appreciably reducing the hazards inherent in current diagnostic measures. Image amplification is a device that permits intensification of the image on a fluoroscopic screen with a much lower radiation dosage than that involved in current standard techniques of fluoroscopy. The adaptation of television devices to make radiography a completely automatic procedure is now under investigation. With such techniques the operator would remain in a completely protected booth, viewing on a television screen the amplified image of what one sees directly under an ordinary fluoroscope. Such devices would permit group consultations with multiple personnel viewing the screen without being exposed to the radiation that they would encounter beside a fluoroscopic table. Perfection of cineradiographic and videotape recording techniques and their adaptation to radiographic procedures will provide further protection to patients, radiographers and radiologists. It is also quite possible that these measures may be adaptable to mass diagnostic radiographic surveys, with a great reduction in the amount of radiation exposure and a consequent lessening of the existing hazards of such surveys.

Dr. F. D. Sowby, Senior Medical Officer, Radiation Protection Division, Department of National Health and Welfare, discussed the principles of radiation protection in the luminizing industry and the use of film monitoring devices among medical and industrial radiological workers. He commented on the results of a recent study in the United Kingdom which indicated that, as compared with a "background" radiation dose of 100 milliroentgens per year, the average citizen in the U.K. receives about 20 milliroentgens per year from medical radiation, of which about 14 milliroentgens comes from diagnostic procedures. It was estimated that if the best possible precautionary measures are scrupulously observed, the latter exposure could be reduced to about 2 milliroentgens per year. This is the ideal situation toward which we should aim.

Many industrial sources of radiation offer a potentially greater hazard than that of medical diagnosis or therapeutic equipment because they cannot be turned on and off with the same precision, they cannot be protected as readily and they can lie around undetected in public places, exposing multiple persons to their emanations. These comments apply to the considerable number of radioactive materials currently employed in industry.

Dr. Sowby observed that anyone desiring to use industrial radiation devices or luminizing procedures such as those employed in the watch and instrument dial industry, must apply to the Department of National Health and Welfare for a licence to do so.

In a survey conducted in recent years by his department, Dr. Sowby reported that among a large number of persons employed throughout Canada in work exposing them to radiation in any form, the highest degrees of exposure were received by industrial workers (men engaged in industrial radiation procedures, and women in the luminizing industry). Appreciably lesser doses were encountered by medical radiological workers. Even among those exposed to higher radiation doses, only a very small number received amounts considered to exceed maximum "safe" levels, and only a small proportion of these required admission to hospital for clinical effects of such radiation exposure. In all of these areas, however, industrial and medical radiation exposure can still be reduced to an appreciably greater degree by better protective measures and by the constant and conscientious observation of precautionary techniques to minimize such exposures.

Dr. G. Stewart, Medical Director of Atomic Energy of Canada, in the final contribution in this session, commented on the hazards of what he termed some "offbeat forms of radiation" such as those encountered in the uranium mining industry and the mysterious cosmic emanations and other forms of ionizing radiation in the upper atmosphere.

The association of bronchial carcinoma with exposure to volatile radon and its daughter substances encountered in uranium mines was first recognized in this century at Joachimstahl and Schneeberg. Gradually, over the years, investigations to establish "safe" levels of exposure to these substances in the uranium mining industry have been carried out and such levels have now been defined by the International Commission on Radiation Protection (I.C.R.P.). Studies throughout Canada's uranium mines indicate that the mine operators have taken the I.C.R.P. safety recommendations seriously and have done a conscientious job of observing precautions to enforce adequate safety regulations in the interests of protection of Canada's uranium miners.

With regard to the radioactive emanations encountered in outer space, Dr. Stewart observed that for practical purposes there is no significant radiation below altitudes of 50,000 feet. At 100,000 feet the biologically effective dose is still less than that considered permissible for industrial radiation workers. However, in contemplated manned space flights of the future, consideration must be given to other forms of intense ionizing radiations that exist in the outer atmosphere in two belts known as the Van Allen zones, so-named after their discoverer. These appear at present

to constitute a major hazard to flight in the outer reaches of space, since adequate protection against them cannot be provided by even the heaviest shielding now available that would be compatible with transit of a vehicle in space.

The effects of cosmic ray particles, as distinct from the radiations in the Van Allen zones, require further study. Cosmic particles can collide with tissue atom nuclei, breaking them up and dispersing them, or heavily charged cosmic particles in penetrating tissues can collide with electrons, leaving a track of quite intensely concentrated ionizing radiation. However, these phenomena are not likely to constitute a significant hazard unless they involve, by a chance direct hit, a vital organ such as the retina or the hypothalamus.

Dr. Stewart predicted that ultimately it will probably become possible for man to penetrate the Van Allen belts and that primary cosmic radiations will not likely constitute an insurmountable hazard to manned space flights, at least to flights of relatively short duration, not repeated frequently by the same personnel.

(To be continued)

MEDICAL MEETINGS

THE TWENTY-FIFTH ANNIVERSARY OF THE CANADIAN PHYSIOLOGICAL SOCIETY

The celebration of the 25th Anniversary of the Canadian Physiological Society was held in conjunction with the 4th Annual Meeting of the Canadian Federation of Biological Societies at the Ontario Agricultural College in Guelph from May 31 to June 2. The beautiful campus of the College formed an admirable setting for this occasion. As with all celebrations, the success of this 25th Anniversary was due in no small part to careful planning and preparation by the organizing committee which consisted of Dr. R. E. Haist and Dr. J. A. F. Stevenson as co-chairmen, Dr. E. Black, Dr. L. P. Dugal and Dr. F. C. MacIntosh, and by the local committee chaired by Dr. H. D. Branion.

The principal event was the conferring of honorary membership on six distinguished scientists: Sir Henry Dale of England, Dr. Laurence Irving of the United States of America, Professor Earl J. King of England, Professor Henri Laugier of France, Dr. E. W. R. Steacie of Canada and Professor A. E. Wilhelmi of the United States of America. All those present at the meeting regretted that Sir Henry Dale, Dr. E. W. R. Steacie and also Dr. F. C. MacIntosh, the President of the Society, were prevented by illness from attending.

A luncheon was held at the Cutten Fields Golf Club on Tuesday, chaired by the Vice-President, Dr. Edouard Pagé. On this pleasant occasion, Professor C. H. Best read a letter of greetings and good wishes from Sir Henry Dale in which he traced the rise of Canadian physiology and its relation to British physiology, as well as recalling the personal pleasure which he had experienced over many years in visiting and being visited by Canadian physiologists both as students and as colleagues. Telegrams of regret and of good wishes for the Anniversary were read from Dr. E. W. R. Steacie and Dr. F. C. MacIntosh.

Professor Henri Laugier, who was introduced by Dr. Eugene Robillard, then gave an inspiring speech. He recalled the great changes in the physical sciences which had occurred during the lifetime of many of his audience and the consequent responsibility weighing upon the scientists in these fields. He emphasized that equally great changes are occurring and will occur in the field of biological sciences, which have led and will lead in the future to increasingly great responsibility for physiologists as "Citoyens Biologistes" not only of their own country but of the world. At the end of the lunch Professor G. H. Ettinger formally requested Dr. Best to convey to Sir Henry Dale the warm appreciation of those present for his gracious letter.

The Canadian Federation of Biological Societies had kindly turned over the annual dinner to the Canadian Physiological Society. This was held in Creelman Hall on the evening of June 1, with Dr. Edouard Pagé presiding. After an excellent dinner, the Chairman recalled something of the history of the Canadian Physiological Society, quoting from the article by Dr. E. H. Bensley which appeared recently in this Journal (84: 1141, 1961). Greetings were then brought by Dr. J. D. MacLachlan the President of the Ontario Agricultural College, Dr. Mark Nickerson, President of the Pharmacological Society of Canada, Dr. Rudolph Altschul, President of the Canadian Association of Anatomists, Dr. Marvin Darrach, President of the Canadian Biochemical Society, and Dr. R. J. Rossiter, Chairman of the Federation Board. Each of these congratulated the Canadian Physiological Society on attaining its 25th birthday and also took some pleasure in pointing out their own ages—younger and, therefore, some of them felt, more lively. Dr. Rossiter drew attention to the role of the Canadian Physiological Society in forming and firmly supporting the Federation in its early days.

Then followed the ceremony of the installation of the honorary members by Dr. Edouard Pagé, the incoming President, and Dr. A. C. Burton, the incoming Vice-President. Certificates and souvenir gifts were presented to each.

Sir Henry Dale was cited as a great scientist and a great man, with a breadth and depth of knowledge and wisdom and with a kindly capacity for making young people feel important. His certificate was received by Professor C. H. Best for transmission to him.

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Dr. Laurence Irving was present at the organizational meeting which led to the formation of the Society and since then has wandered widely geographically and scientifically, his interest leading him from fishes to men and from the tropics to the arctic. He is at present Biologist to the United States Public Health Service at the Arctic Health Research Centre in Anchorage, Alaska, and he has wide interests in scientific adventures in that region. He has an outstanding capacity for friendship.

Professor E. J. King served as secretary of the Toron' Biochemical Society; he worked at the Banting Institute and there carried on his early work on phosphatase, before his traverse to England. Then he developed the productive interest in the biochemistry of disease and in the perfection of analytical methods that has characterized his work ever since. He is Professor of Chemical Pathology at the British Postgraduate Medical School in London. He has been responsible for a great deal of the development and organization of clinical chemistry during recent years. His kindness and the hospitality of his home are well remembered by many Canadian scientists visiting London.

Professor Henri Laugier's scientific interests before the Second World War were in the field of the physiology of work and in physiology as applied to mental health. In 1937 he became Professor of General Physiology at the Sorbonne and also Director of the Centre National de la Recherche Scientifique in Paris. During the war he was a DeGaulle partisan and crossed to the United States, w[illegible] he promoted and urged the cause of France in America. In 1943 he became Professor of Physiology at the Université de Montréal and greatly stimulated the development of this science. He founded the *Revue Canadienne de Biologie*. He was called to be Rector of the Académie d'Alger. He attained high office in UNESCO and finally returned to France and to the Sorbonne. He is a truly outstanding personality and an inspiring and beneficent figure in biological science.

Dr. E. W. R. Steacie is a distinguished physical chemist and a statesman of science. He has for the last nine years been President of the National Research Council of Canada. He is a man whose thoughtfulness, reasonableness, clarity and considerateness have deeply impressed those who read his writings, hear his speeches, or know him personally. The certificate was received on his behalf by Dr. R. F. Farquharson.

Professor Alfred E. Wilhelmi was a graduate of Western Reserve and a Rhodes scholar, and for many years has been a wise and cheerful Associate Editor of the *Canadian Journal of Biochemistry and Physiology*. He has contributed greatly to the development of our knowledge of the biochemistry of anterior pituitary hormones. He is an excellent investigator whose achievements and modesty endear him to those who know him.

Professor Henri Laugier thanked the Society on behalf of all the honorary members.

Dr. R. F. Farquharson, Chairman of the Medical Research Council of Canada, began his speech by recalling the name of Jean Fernel who in the year 1542 when writing a "System of Medicine" called one section "The Natural Parts of Medicine" and coined the word "physiology" for this part of the book, which thus became the first text book of physiology. Dr. Farquharson then went on to trace the develoment of government support for medical research in Canada and outlined in detail the growth of its organization, culminating in the formation of the Medical Research Council in June 1960. He clearly indicated the various types of support available and urged those present to lend their aid in making suggestions for further improvements and increase of flexibility.

On Friday afternoon the Federation Symposium, which had been turned over to the Canadian Physiological Society for the occasion, was chaired by Dr. A. C. Burton and consisted of papers by three of the honorary members.

Professor E. J. King spoke on "Blood and tissue enzymes in the diagnosis and treatment of cancer". Commencing with the acid and alkaline phosphatases and leading on to other enzymes more recently studied in this field, he gave an excellent general review of the subject.

Professor A. E. Wilhelmi spoke on "Extraction of human anterior pituitary hormones" and gave an account of his recent progress in improvement of methods for the separation of growth hormone, gonadotrophins and ACTH in an endeavour to improve the yields and increase the purity of these hormones. Good progress had been made particularly in the case of growth hormone and the gonadotrophins, but the thyrotrophic hormone is still giving great difficulty in its purification.

Dr. Laurence Irving spoke on "Physiological adaptation in arctic life". He described the various ways in which sea mammals, polar bears and other animals were adapted to cold. He discussed in detail observations on variations in the circulation of the hands and feet in Eskimos and others adapted to the arctic climate and showed that, although the adaptation was slight, these changed responses decreased the discomfort and increased the possibility of working outdoors for brief periods with exposed hands. He drew a vivid picture of his work and of life in the arctic. Dr. A. C. Burton thanked the speakers.

Thus ended a most successful 25th Anniversary of the Canadian Physiological Society.

J. S. L. BROWNE

DIVISIONAL MEETINGS OF THE CANADIAN MEDICAL ASSOCIATION, 1961

New Brunswick Division: Algonquin Hotel, St. Andrews, August 30-September 2.

Prince Edward Island Division: Prince of Wales College Auditorium, Charlottetown, August 25 and 26.

Alberta Division: Macdonald Hotel, Edmonton, September 25-28.

British Columbia Division: Kamloops, B.C., October 2-6.

Manitoba Division: Royal Alexandra Hotel, Winnipeg, October 10-13.

Saskatchewan Division: Saskatoon, October 16-20.

CANADIAN SOCIETY FOR CLINICAL CHEMISTRY

The Fifth Annual National Meeting of the Canadian Society for Clinical Chemistry was held at the Ontario Veterinary College, Guelph, on June 2 and 3.

A total of eleven papers were presented during the scientific session, four of these papers being part of a Symposium on Quality Control in the Clinical Biochemistry Laboratory.

B. A. Tobe, of the University of Toronto, reported on the identification and pathological significance of the two components of the blood ammonia level, as determined by the Conway technique.

R. Hobkirk, A. Metcalfe-Gibson and M. Nilsen, of the Montreal General Hospital, presented an exhaustive assessment of the chemical measurement of total estrogens in normal pregnancy urine by Ittrich's direct colorimetric method, and in non-pregnancy urine by Ittrich's fluorimetric procedure, and described a purification procedure to be used in sugar-containing urines.

M. C. Blanchaer, of St. Boniface Hospital, St. Boniface, Manitoba, made a survey of isozymes (serum enzymes that can be resolved into several fractions by electrophoresis), with particular reference to his experience in applying serum lactic dehydrogenase isozyme determinations to routine diagnostic problems.

G. Nadeau and G. Saucier, of l'Hôpital du Saint-Sacrement, Quebec City, discussed the advantages of the intravenous glucose tolerance test for the detection of diabetic and prediabetic individuals.

A. H. Neufeld, of the University of Western Ontario, London, gave a general outline of the nature and characteristics of radioactive isotopes and the uses to which they can be applied in clinical chemistry.

A. Rapoport, of the Toronto Western Hospital, presented a modification of the Howard test for the detection of renal artery obstruction.

D. C. Blood, of the Ontario Veterinary College, Guelph, illustrated the dependence of veterinary medicine upon clinical chemistry as a diagnostic aid, by a discussion of many of the common metabolic and nutritional deficiency diseases of farm animals.

The Quality Control Symposium was conducted by members of the Division of Laboratories of the Toronto General Hospital. D. M. Young, discussing the general problem, stressed the importance of quality analysis and quality controls to patients, clinicians and laboratory workers, and pointed out that an effective program must assess both the accuracy and precision of the results, and evaluate the usefulness of the various chemical determinations which are ordered at the hospital. D. M. Michener-Schatz presented statistically analyzed data on intra-laboratory controls; C. J. Porter discussed data on the overall precision of results obtained in an extra-laboratory control study, and V. R. Waldorf reported on the distribution of laboratory values in health and disease.

Social entertainment included a reception and a banquet, held at the Cutten Golf Course Club House, at which the Warner-Chilcott Lecture was delivered by Professor E. J. King, of the Postgraduate Medical School, University of London, England. Dr. King described the manner in which the professional and organizational aspects of clinical chemistry have been established in England and in most of the major countries of the world. Conducted tours of the Ontario Veterinary College laboratories and small animal quarters were enjoyed by Society members.

At the business meeting of the Society, the following were elected to serve as officers and members of council for the forthcoming year:

President, Guy Nadeau, Hôpital du St-Sacrement, Quebec City; Vice-President, A. H. Neufeld, University of Western Ontario, London; Past President, M. C. Blanchaer, St. Boniface Hospital, St. Boniface, Man.; Secretary, D. B. Tonks, The Hospital for Sick Children, Toronto, Ont.; Treasurer, R. H. Pearce, University of Western Ontario, London. Members of Council: W. F. Perry, Winnipeg General Hospital, Winnipeg; Eleanor Harpur, Montreal Children's Hospital, Montreal; J. D. Taylor, Edmonton; and L. Trochu, Verdun General Hospital, Montreal.

Arrangements for the meeting were under the direction of R. H. Pearce (Chairman), C. Cameron (Local Arrangements) and D. B. Tonks (Program).

As at business meetings of previous years, the primary matter of interest was the discussion of the certification of clinical chemists by the Society, and noteworthy progress was made this year.

REUBEN SCHUCHER, Ph.D.

THE ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF CANADA

SASKATCHEWAN REGIONAL MEETING

The Saskatchewan Regional Meeting of the Royal College of Physicians and Surgeons of Canada will be held in Regina on Thursday and Friday, November 23 and 24, 1961. This is the third of such regional meetings sponsored by the Royal College in its program to provide additional educational opportunities to members of the medical profession engaged in specialist practice.

A cordial invitation is extended to Fellows and Certificated Specialists of the Royal College of Physicians and Surgeons of Canada, living in Saskatchewan, to attend this meeting. Specialists in adjacent areas of Manitoba and Alberta are also invited to attend.

The meeting will be divided into three sections—Medicine and Pediatrics, Obstetrics and Gynecology, and Surgery—and will be held at the Hotel Saskatchewan. The program will include presentations by a number of highly qualified guest speakers.

Fellows or Certificated Specialists of the College desiring to offer papers for presentation should direct their correspondence to the Chairman of the Steering Committee, Dr. C. H. Crosby, c/o Medical Arts Building, Regina. Papers will be limited to 15 minutes. Applications to present papers, accompanied by abstracts, must be submitted to the Chairman of the Steering Committee not later than September 15.

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PUBLIC HEALTH

SURVEILLANCE REPORT OF EPIDEMIC OR UNUSUAL COMMUNICABLE DISEASES IN CANADA

Paralytic Poliomyelitis

Thirty-one cases of paralytic poliomyelitis have been reported in Canada for the period January 1 to June 10, 1961. Quebec and Alberta, with 10 and 13 cases respectively, account for 74% of the Canadian total.

The reporting trend to date is similar to that observed in the low incidence years 1957-58.

Year	*1961*	*1960*	*1959*	*1958*	*1957*
Cumulative total to Week 23	31	171	44	27	29

Indian and Northern Health Services

Shigellosis

An outbreak of bacillary dysentery due to *Shigella flexneri* 2 has been reported at the Nelson House Reserve, Manitoba. One hundred and fifty-four persons were affected out of a total population of 765. The distribution by age group was: under one year of age, nine; 1-5, sixty-six; 6-15, thirty-six; 15 and over, forty-three. There was one death in a three-year-old child.

Typhoid Fever

One case of typhoid fever *(S. typhi O)* in a 23-year-old Indian male has been reported from the Whitefish Lake Reserve, Kinematayo, Saskatchewan. The population of the Reserve is 530. Stools and blood specimens have been collected from family and neighbour contacts. All the water supplies are being tested. The entire Reserve population has been vaccinated with T.A.B.T.

Measles

An outbreak of measles has been reported from the Montagnais Reserve (population 1350) at Bersimis, Quebec. The source of the outbreak was a child returned from a hospital after being in contact with measles. The last measles epidemic in the Reserve was in 1957. Gamma globulin has been provided by the Provincial Department of Health for the younger children in whom complications are feared.

Suspected Rabies

Mould Bay, Prince Patrick Island, N.W.T.—The following incident has been reported from a Canada-United States Joint Weather Station. This station is manned by five Canadians and seven Americans.

On April 16, 1961, a fox attacked a puppy. Two other dogs, kept as pets, killed the fox. The animal was skinned by one of the Canadians and the carcass was thrown on the garbage dump. On May 5, the puppy bit one of the Canadian employees on the thumb. The following day the puppy became listless and behaved unusually, and on May 7 had a fit. On the advice of the R.C.M.P. Resolute Bay Station, the dogs were shot and arrangements were made for the air evacuation of the two Canadians and the puppy to Thule Military Hospital, Greenland. The puppy died on May 7 at Thule, with clinical signs of rabies. The two Canadians were started immediately on rabies vaccination. On May 10, Dr. J. A. Hildes from the University of Manitoba proceeded to the base and on May 12 one Canadian and two Americans were evacuated to Winnipeg for rabies vaccination (chick embryo vaccine).

The heads of the two dogs were sent to the Health of Animals Pathology Laboratory, Hull, Quebec. The search for Negri bodies proved negative and so did the mouse inoculation tests. The puppy's head was sent to Lackland Air Force Base, Texas, where it proved negative for Negri bodies and fluorescent-antibody-antigen tests. Mouse inoculation proved negative for rabies although some animals did die. No information is available on the cause of death of the puppy.

Infectious Hepatitis

Five cases of infectious hepatitis have been reported from Kuper Island, British Columbia, two at the Indian residential schools and three in private families. The 160 residents of the school and the other members of the families have been given gamma globulin.

Trichuriasis

A case of whipworm disease has been reported from Castlegar, British Columbia, in a 6-year-old boy. The family of the patient arrived there recently from Portugal. A sister of the boy is suffering from amebiasis.

Trichinosis

Three more cases of trichinosis have been reported in the Abbotsford area of British Columbia. The first case was reported during April.

Streptococcal Sore Throat

An outbreak of streptococcal sore throat has been reported in a school at Slave Lake, Alberta. One hundred and eighty children have been affected, representing about 60% of the school population. The outbreak has spread with great rapidity within two weeks, necessitating the closing of the school. Penicillin is being administered therapeutically and prophylactically.

Gas Gangrene

A case of gas gangrene has been reported from Olds, Alberta. After a car accident the patient sustained a compound fracture of the right foot and multiple lacerations. He was transferred to the University Hospital in Edmonton following treatment at the local hospital consisting of debridement and reduction, 2,000,000 units of penicillin, one g. of chloramphenicol intravenously and 5 ampoules of gas gangrene antitoxin.

Tularemia

A case of tularemia in a 20-year-old male has been reported from Elk Point, Alberta.

Epidemiology Division, Department of National Health and Welfare.

Ottawa, June 17, 1961.

CHANGE OF ADDRESS

Subscribers should notify the Canadian Medical Association of their change of address one month before the date on which it becomes effective, in order that they may receive the Journal without interruption. The coupon on page 33 is for your convenience.

GENERAL PRACTICE

THIRD CONGRESS OF GENERAL PRACTITIONERS OF THE INTERNATIONAL COLLEGE OF GENERAL PRACTICE

MEMBERS of the College of General Practice of Canada are invited to attend the Third Congress of General Practitioners of the International College of General Practice, to be held in Salzburg, Austria, from September 11 to 14, 1961. The preliminary program follows:

September 11

Morning: Announcement of winners of the Winthrop Prize; "Ethics and the General Practitioner"—Schulten; "Does the General Practitioner Still Perform a Function of Importance?"—Franz; "Cancer Detection in General Practice"—Loeb.

Afternoon: Third General Assembly of the International College.

Evening: Civic Reception at the Schloss Mirabell, Salzburg.

September 12 (Morning)

"The Gynecological Examination in Diagnosis"—Brandt; "Unusual Sites for Pain in Influenza and Colds as a Precursor of Further Illness"—Geiger; "Therapeutics in General Practice"—Lüth; "The Necessity for Theoretical Considerations in Everyday Practice"—Schlegel.

September 13 (Morning)

"The Evaluation of General Practice Records"—Prosenc; "Letters Concerning Patients (The Doctor's Report)"—Neumann; "Special Terms in Research in General Medical Practice which are Important to the General Practitioner"—Brandlmeier; "Diagnostic Distortions"—Kidd.

September 14 (Morning)

"The Treatment of Old People by the General Practitioner"—Szakolyi; "The Classic Symptoms of Diabetes Mellitus as seen in the Office of the General Practitioner"—Krause; "Special Cardiologic Terms in Clinic and Medical Practice"—Halhuber; "Ulcer Disease in Young Adults and Children"—Lachner.

BOOK REVIEWS

WORLD REVIEW OF NUTRITION AND DIETETICS. Vol. II. Edited by Geoffrey H. Bourne. 247 pp. Illust. Hafner Publishing Company Inc., New York, 1961. $9.50.

The impressive list of renowned nutritionists from France, Africa, U.S.A., New Zealand, Sweden and Switzerland, who have contributed to this volume, speaks for itself in establishing this text as one of worthwhile repute.

The book includes the following topics of current interest in nutrition: proteins and hematopoiesis; the effect of malnutrition on the eye, with special reference to work with experimental animals; dietary factors and adrenocortical hormone secretion; microbiology of digestion; vitamin interrelations of ascorbic acid; role of carotene and vitamin A in animal feeding; parathyroid glands and calcium metabolism; vitamin-D deficiency and bone and tooth structure; and fluorine.

The work which is discussed under each of the above topics illustrates very emphatically the importance of considering the interrelationships of the nutrients in interpreting any effects of malnutrition. In addition to this, the interrelationship of nutrients with the endocrine and enzymatic functions of the body is discussed under several headings.

The chapter on microbiology of digestion is of interest in that this subject is not generally treated under one heading. Much of this information is scattered throughout the literature under the headings of specific nutrients, and it is both convenient and informative to have it consolidated in one chapter.

For the convenience of those who might be interested in investigating further any of the topics discussed, each chapter has a most satisfactory reference list.

Another informative feature of the text is the inclusion of several excellent plates to illustrate the physiological effects of some of the types of malnutrition discussed.

The biochemical, physiological and histological aspects of the science of nutrition that form this treatise make this a valuable text for the medical profession as well as those occupied with teaching and research in nutrition.

CANCER: DISEASE OF CIVILIZATION? Vilhjalmur Stefansson. 180 pp. Hill and Wang, New York; Copp Clark, Toronto, 1960. $4.50.

" . . . accounts of regions and peoples free from cancer deserve attention, for they indicate a correlation between civilizational noxae and cancer" might well stand as the text to which Stefansson has oriented this assembly of evidence. He quotes this passage from "Cancer: Its Nature, Cause and Cure", by Dr. Alexander Berglas of the Cancer Research Foundation, Pasteur Institute, Paris (1957).

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To point to the correlation and to provide a base for a hypothesis, Stefansson utilizes two unique qualifications: his own direct observation of Arctic primitives through more than ten years of living with them; his half-century of experience in epistemology and his masterly technique of extracting and highlighting significant elements in complex documentation. With imposing data from authorities on Arctic peoples, the author presents corroborative findings on the Hunzas (the cancer-free people of Asia); Indians of Bolivia, Brazil and Ecuador; and Negroes of Central Africa. There seems little room to question the validity and the pertinence of the reported observations. There seems no room to evade giving them attention.

The present incidence of cancer surely demands that no possible line of defence or attack be neglected. It may be that careful consideration of the anthropological view of "Man's place in nature" could generate strategic concepts of prevention within which the tactical weapons of laboratory, clinic and operating room need be called on with a decreasing rate of frequency. René Dubos, of the Rockefeller Institute, so implies in the concluding sentence of his laudatory Introduction: "It is the responsibility of social and medical sciences to analyze the natural and artificial forces which affect [modern man's] health and happiness, in order to help him develop a rational way of life fitted to the new world he is creating."

IMPRESSIONS OF EUROPEAN PSYCHIATRY. Walter E. Barton, Malcolm J. Farrell, Frances T. Lenehan and William F. McLaughlin. 128 pp. American Psychiatric Association, Washington, D.C., 1961 $4.00.

This book contains the full report of a team of three American psychiatrists and one psychiatric nurse who recently visited 47 psychiatric institutions in Great Britain, Belgium, Denmark, France and Holland. They discuss such diversified topics as: respect for the patient as an individual; public attitudes toward mental illness; sociocultural factors in treatment; the impact of national health programs; community psychiatry's functions; administrative principles and policies; traditions and developments in nursing; training practices in psychiatry; specialized facilities and treatment programs; therapeutic philosophy and treatment methods; nature and extent of rehabilitation; programs and progress in research, and unsolved problems and future trends.

Their comparison between the situation in the abovementioned European countries and the United States appears as unbiased and objective as possible under the given circumstances. J. Mackenzie of Boston adds his own observations made during his participation in the teaching program in the University of Aberdeen Medical School, Scotland.

This report is a valuable contribution to the mutual understanding between Europe and the American continent in the vast and increasingly important field of psychiatry. Some questions, however, might enter the mind of readers well acquainted with Europe and its psychiatric institutions: Are these five countries really representative of Europe? Are the writers of this report not a little too optimistically impressed by what they saw and studied? Were they shown the "back wards" of some psychiatric institutions? Perhaps the answers to these and similar questions might be found in future studies of this kind.

SYNOPSIS OF HISTOLOGY. Henry J. Werner. 149 pp. The Blakiston Division, McGraw-Hill Book Company, Inc., Toronto, 1961. $4.25.

This manual is a skeleton of histology, stripped of its flesh and exciting implications, and as a histological concentrate it is about as palatable as K-rations. However, according to the author it is not intended as a text or reference work but rather "(1) to facilitate the recognition of histological sections, (2) highlight salient features of cells, tissues, and organs, and (3) to serve as a concise source of review in times of 'emergencies'."

The outstanding features of the work are the broad scope of the material covered and the author's originality of phrase and organization.

There are some minor omissions (for example, myeloid tissue is barely mentioned and there is no account of hemopoiesis) and some details have been included which might well have been omitted. There are several minor inconsistencies and errors.

Many of the descriptions and definitions are too brief to evoke or recall mental images of structure and there are no illustrations to supplement these deficiencies.

The book is of an awkward size—too large for the pocket and too small to be a notebook. Being paperbacked it would probably not stand up under the wear and tear of daily use. Because of these limitations it is doubtful whether the author has achieved the first two of his objectives.

However, the book compares favourably with similar outlines of histology. The material is well organized, the type though small is clear, and the index is adequate. The exclusion of illustrations doubtless reduces the cost of publication, so that the book should be within the means of every student. Consequently, this synopsis of histology should prove useful and appeal to students as a means of reviewing in preparation for examinations in histology and thus fulfil the author's third objective.

ROENTGENOLOGY OF INTRACRANIAL MENINGIOMAS. Sidney P. Traub. 238 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. $14.00.

"Roentgenology of Intracranial Meningiomas" is a review and analysis of the clinical records and roentgenograms of 170 cases of meningioma at the Montreal Neurological Institute plus 17 cases at the University Hospital, Saskatoon. The contents of the book are well organized. It commences with a short historical review of meningioma, age and sex incidence, clinical observations and the pathological aspects.

The main portion of the book is concerned with changes that may be seen on the plain roentgenograms of the skull. The author deals first of all with nonspecific changes suggestive of a space-occupying intracranial lesion. He next deals with specific changes which are suggestive of meningioma. The reproductions of the x-ray films in this section are very good. It is of considerable interest to note that 88% of the patients in his series showed some abnormal changes on the skull roentgenograms. Almost 35% showed a specific change very suggestive of meningioma. This, of course, re-emphasizes the tremendous importance of taking plain films of the skull in cases of suspected meningioma.

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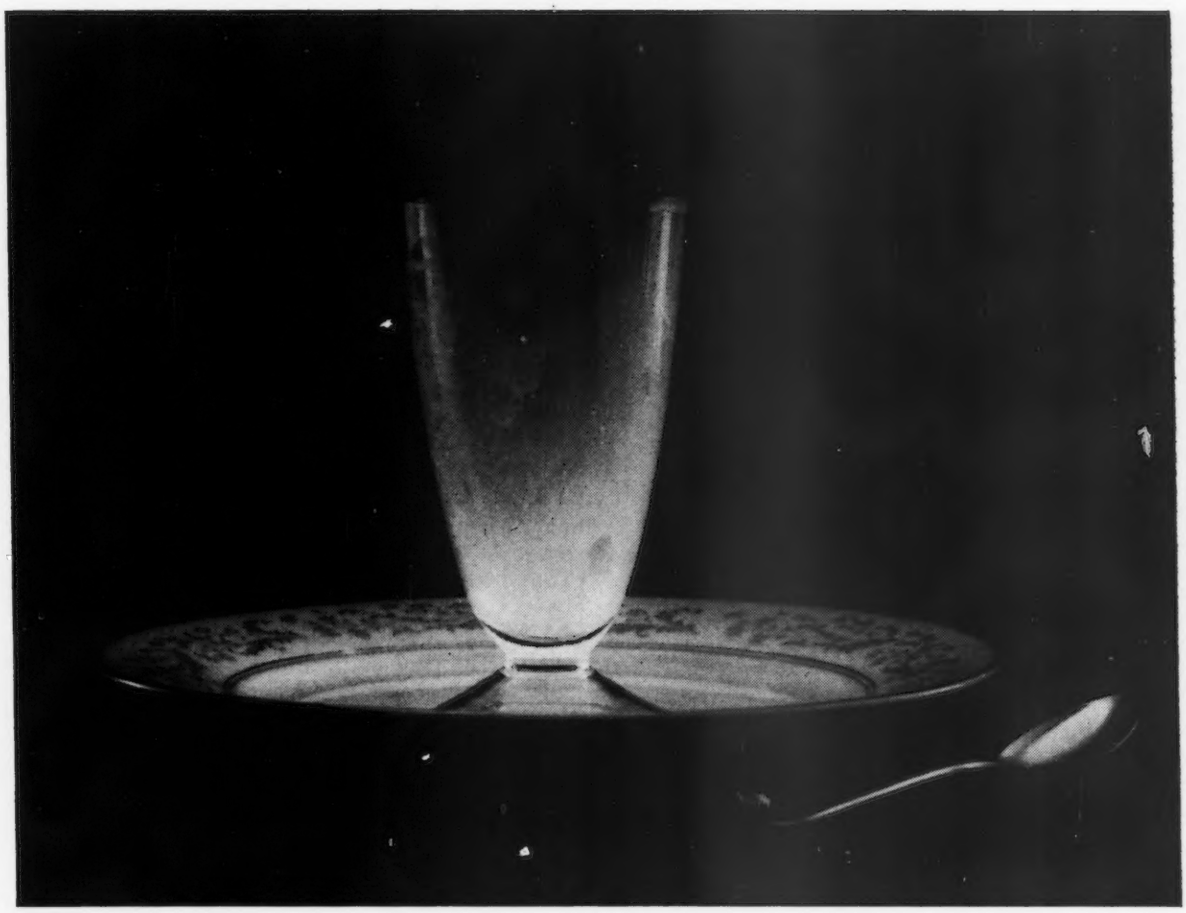

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The section on pneumoencephalography could be longer. Some recent work which has been done on encephalography and posterior fossa meningioma has not been included. However, most of the main findings using air studies are very adequately described.

Cerebral angiography was used on only seven cases in the series. One must remember, however, that many of the cases which the author is reviewing were seen considerably before cerebral angiography became a common procedure. There are excellent reproductions showing many of the changes in the vascular supply to meningioma.

Chapter X summarizes the clinical and roentgenologic features of the various forms of meningioma very adequately. There is also an excellent bibliography at the end of the book.

The publishers are to be complimented on the excellence of the reproductions of the roentgenograms.

This book stresses clearly the great importance of plain roentgenograms of the skull in the diagnosis of intracranial meningiomas. The chapters on pneumoencephalography and cerebral angiography show the value of these procedures. This is a book well worth reading by neurosurgeons, neurologists and radiologists interested in meningiomas.

THE AIR WE BREATHE. A Study of Man and His Environment. Edited by Seymour M. Farber and Roger H. L. Wilson. 414 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. $14.00.

This book represents a co-operative approach to the portrayal of recent knowledge concerning the atmospheric environment of man and the resultant effects of exposure to contaminated atmospheres. This has been accomplished by a group of experts and specialists in the fields of medicine, public and occupational health, biometry and statistics, chemistry and physics. The material consists of a collection of scientific papers and panel discussions presented at a recent international symposium held at the University of California Medical Center at San Francisco. Information on various aspects of the subject is presented in sections dealing with the "normal" atmosphere and its variations; the air pollution problems of industry; urban living under smog and fog; and specific problems such as the relation of dusts and other suspensoids to lung cancer.

There are some outstanding chapters in the book, among which may be mentioned those that describe the influence of climatic stress on human activity, the physiological effects of altitude, the behaviour of dust particles in the respiratory system in relation to disease, the experimental approach to lung cancer and the chapters dealing with smoking and other airborne factors in lung cancer. Those readers who are experimental investigators or who desire more background information on original research work will welcome the inclusion of references to source documents and scientific papers which are listed at the end of each chapter.

This book should be a welcome addition to libraries and useful to general practitioners and other members of the medical profession, and to scientists and engineers who are interested in the subject of air pollution and the effects on man of his atmospheric environment. The presentation and style are relatively simple; little of the material can be considered trivial in nature and much of it could be understood even by the lay reader.

MULTIPLE SCLEROSIS: PROGNOSIS AND TREATMENT. American Lecture Series. Leo Alexander, Austin W. Berkeley and Alene M. Alexander. 188 pp. Illust. Charles C Thomas, Springfield, Ill., 1961. $7.50.

This monograph records the work of a special clinic for patients with multiple sclerosis. It is mainly a report on the prognosis of the disease and on the value of certain treatment methods, based on observations on more than 500 patients.

An acute description of difficulties in diagnosis, and of details of age, sex incidence, and other variables, is provided. Then follows the scoring method, upon which the statistical analyses depend. A point allocation system is used to cover all the common symptoms and signs, the results of successive examinations being thus reduced to numeral scores which indicate progress or regression in relation to time and treatment. The point system is detailed and said to tally well with clinical impressions; moreover, unjustified precision is not claimed. Nevertheless the point value of a symptom or sign is necessarily arbitrary: sensory changes, for instance, seem to have been assigned less than their share.

The remainder of the book is a detailed and critical statistical analysis applied to episodes of the disease, to its course, and to treatment by blood transfusion, ACTH, or adrenal cortical steroids. The methods and language may not be familiar to clinicians but the discussion is convincing and the critical attitude reassuring.

This is a worthwhile monograph, with much useful information and with statistical conclusions which the clinician will probably accept though he may not understand.

CARDIOPERICARDIOMYOPEXY. New Surgical Treatment for Heart Diseases. Dr. Aaron N. Gorelik in collaboration with Prof. Camille Lian, Prof. Louis Thieblot, Dr. Mendel Jacobi et al. 176 pp. Illust. Myopexy Association Inc., New York, 1960. $5.00.

This book is divided into six chapters, the first of which, written by Dr. Gorelik, concerns cardiopericardiomyopexy as a surgical treatment for revascularization of the myocardium. The other chapters, written by associates, pertain to: (1) diagnosis of heart disease, (2) physiology of the coronary arteries, (3) pathological findings, (4) anesthesia and (5) uses of xylocaine.

Gorelik points out that coronary artery insufficiency frequently manifests itself in symptoms of weakness and susceptibility to fatigue, in addition to the well-known symptoms of angina and dyspnea. He terms this clinical picture "myocardial asthenia". He states that a damaged myocardium cannot be replaced and urges early operation. He is of the opinion that coronary arteriole changes are part of a generalized arteriosclerotic process which he believes involves metabolic disturbance of the thyroid, pancreas, liver and kidney as well as allergic manifestations.

His concept of the etiology of coronary arteriosclerosis appears to be somewhat complicated.

Gorelik states that patients suffering from rheumatic valvular disease with myocarditis and patients with congenital ventricular septal defects suffer from coronary artery insufficiency either because the myocardium has hypertrophied or because the rheumatic fever process has involved myocardial arterioles.

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Thus he believes that such patients would benefit from myocardial revascularization in the same way that patients with coronary artery insufficiency benefit from coronary artery surgery.

A report is given of 130 patients operated upon by his technique of cardiopericardiomyopexy which, fundamentally, involves the introduction of magnesium silicate powder into the pericardial sac. He reports a 5% mortality with this procedure and states that all patients who survived the operation are well and able to resume normal physical activity. He also reports operating on 64 patients suffering from rheumatic heart disease such as mitral stenosis, mitral insufficiency and auricular fibrillation with a 9% operative mortality and a very marked improvement in the ability of these patients to exercise following this revascularization procedure without any correction of the underlying valvular lesion.

The chapter by Louis Thieblot is quite interesting.

A chapter on pathology by Jacobi describes considerable vascularity in two cases examined following cardiopericardiomyopexy, but the reproductions of the photomicrographs of the vascularized areas do not convince one that there are pericardial-myocardial-vascular connections larger than capillary size and these have not been demonstrated in any large number.

No fresh evidence concerning the value of cardiopericardiomyopexy in the treatment of myocardial ischemia has been brought forth to indicate that this type of procedure is capable of increasing myocardial circulation by introducing extracardiac blood into the myocardium.

MEDICAL AND BIOLOGICAL RESEARCH IN ISRAEL. Edited by Moshe Prywes. 562 pp. Illust. The Hebrew University of Jerusalem, Jerusalem; Grune & Stratton, Inc., New York, 1960. $8.00.

An attempt has been made to survey the achievements in medical and biological research in Israel from the time of the nation's inception in 1948 to the present. The first half of the book concerns itself with science as applied to the survival of a small nation, poor in natural resources and beset with the social, nutritional and medical problems related to the integration of a heterogenous group of one million new immigrants of varied cultural and economic backgrounds and ranging geographically from Europe to India. The control measures against insect pests and tropical and Middle Eastern disease such as malaria, trachoma and bilharziasis are well discussed and the difficulties faced by a European population struggling to adapt to a tropical environment and an Oriental population to a European culture are pointed out. Agricultural and industrial progress are discussed and the many problems yet to be solved are sharply revealed.

The latter half of the volume discusses the fundamental research that has taken place in cancer, genetics, microbiology and medicine. The reader is struck by the fact that a nation existing on the brink of national disaster can allow itself the luxury of such extensive basic research.

The material presented in this book is well organized but is so vast that most subjects are only briefly covered. A bibliography of 2000 references acquaints the reader with the otherwise little known scientific literature of Israel.

DIE INTERSEXUALITAET. Prof. Dr. Claus Overzier. 560 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany, 1961. $28.35.

This book offers an up-to-date review of the problems related to intersex. It will be of great value to medical practitioners, geneticists and pathologists as a basic textbook on the subject and particularly as a remarkable source of references. These fortunately are always quoted with their full title. The various subjects are treated by well-known experts and include the scientific and theoretical basis as well as the clinical and laboratory aspects of intersex. The embryology, animal experiments, chromosomal studies, laboratory procedures for routine determination of nuclear sex, the role and evaluation of hormones and the clinical approach to patients are discussed in a concise and comprehensive manner. Testicular feminization, Klinefelter's syndrome, gonadal dysgenesis and adrenogenital syndromes are presented in detail. This applies also to the hormone-producing tumours and the nuclear sex of tumours in general. It is unfortunate that the chapter on pseudohermaphroditism is very short; for clinicians particularly, a more extensive discussion of this subject would have been desirable. Genital anomalies not related to intersex, plastic operations and psychiatric aspects are also briefly reviewed. A helpful feature for those who have little time for reading is the sufficiently detailed summaries at the end of each chapter. The illustrations are numerous, well chosen and of good quality. With the exception of the chapter on psychiatric problems the German is such that the reading of this book will not present any difficulty to those who know this language fairly well.

THE CHEMISTRY OF BRAIN METABOLISM IN HEALTH AND DISEASE. A Monograph in The Bannerstone Division of American Lectures in Living Chemistry. J. H. Quastel and David M. J. Quastel. 170 pp. Charles C Thomas, Springfield, Ill., 1961. $6.50.

The authors of this excellent little monograph could not be better qualified for their job. The senior author is a world-renowned neurochemist; the junior author, his physician son, rounds out the background of the team. Medical books nowadays tend to be weighty and undiscriminating tomes; thus, it is particularly refreshing to pick up a book which covers an extensive topic well, yet can be easily read in an evening. The book faithfully accomplishes the objectives set forth by the authors in the preface, which is to provide a "brief survey of the chemical processes that take place in the brain during health and cerebral disease". Unfolded before the reader, in concise and orderly fashion, is the normal chemical machinery of the brain, and the manner in which many pathological processes disrupt this machinery becomes readily apparent. The subject matter is amply documented with 524 references to the literature extending through 1959 (the one 1960 reference is to a paper by one of the authors).

Unfortunately, the book competes closely, both in content and scope, with one by H. McIlwain, published in 1959 with references through 1958. In both cases it is the classical portion of neurochemistry which is most ably presented. Readers may be disappointed, as was this reviewer, in the presentation of material on the metabolism of the central amines and the relationship to the newer psychoactive drugs. This area forms

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the major application of neurochemistry to medicine today, and is one of the most fascinating and rapidly advancing areas of medical science. The subject matter might have been considerably expanded and presented in a single chapter instead of being included as disconnected parts of three chapters. The book can nevertheless be recommended to physicians, students, and scientists of various disciplines who have an elementary knowledge of biochemistry and wish an introduction to the subject of neurochemistry.

PSYCHIATRIE. Ein Lehrbuch für Studierende und Aerzte. 5th revised ed. Kurt Kolle. 418 pp. Illust. Georg Thieme Verlag, Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1961. $7.10.

This work has become the representative textbook of psychiatry for students, practitioners and budding psychiatrists in Germany. The author, professor of neuropsychiatry in Munich, who counts Kraepelin, Hoch and other important psychiatrists among his predecessors, has ample opportunity to show his great teaching skill and experience as well as his large horizon. Although not dynamically oriented himself, he gives the psychoanalytic and related schools of thought fair consideration. His main goal is the integration of psychiatry in the great edifice of medicine and humanity without which success and progress are unthinkable.

The text is divided into four large parts. Part one contains a general introduction and deals with two large topics: man as a subject of psychiatry and psychic abnormality. Part two, special psychiatry, deals with the topics of abnormal personalities, psychic crises (neuroses, psychogenic reactions), obsessive illness, mental retardation, the cyclothymic and the schizophrenic groups, epilepsy and other conditions associated with seizures, general paresis, brain diseases associated with psychic disturbances, symptomatic psychoses (exogenous reaction types), addictions and child psychiatry. Part three, applied psychiatry, presents the practical aims of psychiatry, social and forensic psychiatry, and the examination of the psychiatric patient. Finally, part four, under the heading of scientific psychiatry, deals with psychiatric diagnosis, system and research, and contains a table of important historical data concerning psychiatry, from Pinel who freed the mentally ill patients from their chains, to the year 1952, when the French psychiatrists Delay and Deniker initiated psychopharmacology.

This book is interesting and readable from cover to cover, and represents a rich source of information and reference.

DEW LINE DOCTOR. G. Howard. 191 pp. Illust. Robert Hale Limited, London, 1960. $2.50 (approx.)

The doctor-author of this book began work in Canada selling sports equipment in a Montreal department store where he heard about the DEW Line. Applying to the medical superintendent of the construction company holding the four hundred million dollar contract, he found himself in ten days on the way to Baffin Island, a place that seemed like the end of the earth.

His practice covered an area of 600,000 square miles, inhabited by DEW Line construction workers and Eskimos. Though much of his diagnosis and treatment was done by teletype, he made visits by dog team, snowmobile and mostly by plane.

He learned to respect the Eskimos, who live hard lives without complaint though none today starve to death. Infanticide has died out because of government aid in needy cases and because of the family allowances, as has the custom of abandoning the aged to die when they can no longer help to support the community.

He treated a variety of acute medical conditions, many accidents and coped with cases of the Arctic blues. His days were brightened by the humour of the keen young workers, the kindness of the nurses, the dignity of the Mounted Police and the faithfulness of the Anglican and the Roman Catholic missionaries.

He stayed on through the summer watching the profusion of the summer blossoms and the large numbers of migratory birds. During his term the Council of the North West Territories chose their national flower, the Mountain Avens (*Dryas integrifolia*).

This is a horizon-enlarging book for both lay and medical reader.

DIE ŒDEME. Physiopathologie und Therapie de Salz und Wasserretention. Jean Fabre. 256 pp. Illust. Benno Schwabe & Co. Verlag, Basel, Switzerland, and Stuttgart, W. Germany; Intercontinental Medical Book Corporation, New York, 1960. $9.50.

This medium-sized book on edema has a number of advantageous features for the reader who is not actively engaged in research in this field. As it represents the analysis and synthesis of modern knowledge by a single author, it can be read from cover to cover with sustained interest. Thus the arrangement of the chapters, beginning with the physiology of salt and water excretion, followed by the pathological physiology of edema leading to chapters on diuretic therapy, which deal in fine detail with low salt diet and the entire spectrum of diuretics, achieves the purpose of communicating the information effectively. The book was originally written in French but it was revised and "rendered" into German by the co-operative effort of the author and two associates, the latter also intimately familiar with the subject matter.

Some points are treated with greater emphasis by this European author than they receive in North America. A notable example is the concern about the tendency of mercurial diuretics to enhance thrombus formation. The author states that he routinely administers anticoagulants before and during treatment with mercurials. In some cases of congestive cardiac failure diuresis may be enhanced by bleeding. This is explained by invoking Starling's law; the reduction in blood volume results in shortening of myocardial fibres and improving cardiac function. In the opinion of this reviewer, these two features do not merit such emphasis.

In the short last chapter the author presents the special indications of the various diuretic agents and methods and the cryptic elements which make for "refractory" edemas and how to deal with them. He also sounds a note of caution, *primum nil nocere;* the toxic side effects of each therapeutic measure must be kept in mind to avoid doing more harm than good.

The references to the literature number 960 and include the works of the pioneers in each facet of the subject. A good index adds to the effectiveness of the book, which is written in a graceful style.

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MEDICAL NEWS *in Brief*

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CAUSE OF DISABILITY AMONG EMPLOYEES

Respiratory ailments rank first among the causes of disability lasting eight days or more among employees of Metropolitan Life Insurance Company, it is reported by the company's statisticians.

The incidence rate of such disability in 1960—156 per 1000 personnel—was about the same as the two preceding years. However, there were contrasting trends in the disability rates for the two sexes. Among males the rate decreased steadily from 114 per 1000 in 1958 to 107 in 1960, while among female employees it rose from 228 to 237 in the same period.

Women have higher disability rates than men throughout the main working ages, but the degree of disparity varies with age. Disability rates are 1 2/3 times as high for women as for men under age 25 and about 3½ times as high as for men at ages 25-44.

Diseases of the digestive system ranked second to respiratory diseases as a cause of disability among both men and women. Accidental injuries ranked third among women and fourth among men. Diseases of the circulatory system ranked third among men, but was well down the list for women.

NUTRITION SOCIETY OF CANADA

At the Fourth Annual Meeting of the Nutrition Society of Canada, held at the Ontario Agricultural College, Guelph, on May 30, the following officers were elected: President, Dr. E. H. Bensley, Montreal; Vice-President, Dr. R. H. Common, Macdonald College; Treasurer, Dr. J. A. Campbell, Ottawa; Secretary, Prof. E. V. Evans, Guelph; Councillors, Dr. J. M. Bell (1964), Saskatoon, Dr. L. P. Dugal (1963), Ottawa, and Dr. W. W. Hawkins (1962), Halifax. Professor J. Biely of Vancouver is Past President.

A feature of the annual dinner of the Society was the announcement of the winner of the second Borden Award of the Nutrition Society of Canada for research in nutrition. This year's winner, Dr. Donald Fraser of the Research Institute, Hospital for Sick Children, Toronto, was cited for his work on vitamin D-refractory

rickets in children and on various aspects of calcium and phosphorus metabolism.

The special speaker at the dinner was Dr. Ross A. Chapman, Assistant Director, Scientific Services, Food and Drug Directorate, Ottawa, whose topic was "Research in the Food and Drug Directorate". The one-day Society program included a session of short research papers and a symposium on "Current Problems in Nutrition". Registered attendance at the meeting was 88 members and visitors.

THE VITAMIN MANIA

In the face of the endless barrage of inflated advertising claims about the benefits of vitamin ingestion, regular warnings from the medical profession about the limited clinical indications for vitamin supplements are needed. C. S. Davidson, in an editorial entitled "Vitamins: Charms or Nutrients" (*J. A. M. A.*, 176: 869, 1961), strikes a familiar but necessary note. Many vitamins are known to be required by man and some, in large doses, may be toxic. Most of them have intracellular metabolic activities as coenzymes. However, the important truth is that normal individuals eating a variety of nutritious foods need no prophylactic or therapeutic vitamins or minerals. It is dangerous, although easy, to prescribe vitamins for symptoms due either to the subtle beginnings of serious illness or to functional complaints. Vitamin administration should never be a substitute for care in diagnosis, nor should vitamins ever be used in lieu of careful search for other causes of the patient's symptoms and signs. If after careful study of a patient, however, it is found that deficiency states may be present, or are likely to arise, judicious prescription of vitamin mixtures is necessary and proper therapy.

The use of vitamins as placebos or to fortify suggestion in treating a psychoneurotic patient is probably a frequent practice in spite of its cost. The physician who uses vitamins as placebos should, perhaps, be thankful to vitamin promoters for making these charms so real and therefore giving them additional effectiveness. He must not, however, believe that jangled nerves, malaise, depression, anemia, and other symptoms that are hard to explain, are the result of vitamin deficiencies. He must study his patient carefully and must also learn the

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true nature and effectiveness of vitamins. This is a steadily growing subject that requires careful and continued study by every physician. If he has done these things, the physician is in a position to advise and treat his patients effectively. Then, if he should choose to take advantage of the health superstitions and use vitamins for their placebo effect, the physician has made a positive decision and is not deluding himself.

AMERICAN FRACTURE ASSOCIATION—22ND ANNUAL MEETING

The Twenty-Second Annual Meeting of the American Fracture Association will be held in the Shoreham Hotel, Washington, D.C., from September 16 to 23, 1961.

Sunday, September 17, will be devoted to a Postgraduate Course in Orthopedic Surgery and Fractures, which will be held in the Gorman Auditorium, Georgetown University School of Medicine, Washington. The tuition fee of $10 includes lunch and bus transportation to and from the hotel.

The remainder of the scientific program in the Shoreham Hotel, beginning on Monday, September 18, will feature symposia on "Supracondylar Fractures of the Femur", "Fractures of the Hand", "Fractures of the Distal End of the Radius" and "Fractures of Condyles of the Tibia"; X-Ray Forums for discussion of interesting problem cases; a Round Table Luncheon providing for simultaneous discussion of ten separate subjects; approximately 20 individual papers; tours of the Walter Reed Hospital, Armed Forces Institute and National Institutes of Health; scientific exhibits on "Extraskeletal Fixation", "Hege Pins" and "Fractures of the Shaft of the Tibia"; and an extensive social and entertainment program.

The Chairman of the Annual Meeting is Dr. Milton C. Cobey of Washington, D.C.

LEAD PAINT POISONING IN CHILDREN

Lead paint poisoning in children caused by ingesting paint containing this metal is preventable. Public health authorities are taking steps to prohibit the interior painting of dwelling units with such paint and are removing it under nuisance abatement powers. In a recent publication Kaplan and Shaull (*Am. J. Pub. Health*, 51: 65, 1961) describe a simple and inexpensive procedure for rapidly screening paint scrapings to determine compliance with regulations which require warning labels on paint with lead in excess of 1%. The procedure used for the rapid screening of paint scrapings at the 1% level in order to determine whether or not the newer regulations for control have been followed, should be valuable to the public health worker, sanitarian and epidemiologist.

REFRESHER COURSE IN MALIGNANT DISEASE, BRITISH COLUMBIA CANCER INSTITUTE

A Refresher Course in Malignant Disease, sponsored by the British Columbia Cancer Institute, will be held in Vancouver from October 10 to 13, 1961. The guest speakers will be Sir Stanford Cade and Sir Peter Dixon, of London, England, and Dr. Arthur T. Hertig, Boston, Mass.

Applications should be addressed to: Dr. A. M. Evans, Director, British Columbia Cancer Institute, 2656 Heather Street, Vancouver 9, B.C. There is no fee.

STATISTICS ON HEART DISEASE

Arteriosclerotic heart disease, including coronary disease, is responsible for more deaths in the United States than all other types of heart diseases combined, according to statisticians of Metropolitan Life Insurance Company.

The disease varies in relative importance in the major segments of the population. Arteriosclerotic heart diseases account for almost four-fifths of all heart disease deaths among white males, for two-thirds of those among white females, for slightly over half of those among non-white males, and slightly less than half among non-white females.

The proportion of deaths ascribed to this leading type of heart disease increases with advance in age, the rise being particularly rapid during early adult life. For example, among white males somewhat over half of all heart disease deaths at ages 25 to 34 are of the arteriosclerotic type, the proportion increasing to nearly 80% at 35 to 44 years and to about 85% in the 45 to 64 age range, after which it decreases moderately. This

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pattern holds true for other segments of the population except non-white females, where the highest proportion is among the age group 75 and over.

Second in numerical importance is hypertensive heart disease. It causes only 7% of all heart fatalities among white males, and about twice that proportion among white females. It is of relatively much greater importance among non-white persons, accounting for a little more than one-fifth of all heart disease deaths among males and for almost one-third among females.

Although the mortality from rheumatic heart disease was much higher a generation ago, it still ranks as a major cause of heart disease fatalities in childhood and early adult life.

Most of the cardiac deaths among infants and young children are of congenital origin. Congenital heart disease takes so large a death toll in infancy that the mortality rate from heart disease as a whole under age one is higher than that for any other age group under age 45.

"The current pattern of heart disease mortality with respect to type does not appear likely to change materially in the near future," the Metropolitan statisticians conclude. "Unless there are major advances in the prevention and treatment of arteriosclerotic heart disease, and more particularly coronary artery disease, this type will remain the dominant item in the heart disease picture."

1963 MOYNIHAN PRIZE

The Association of Surgeons of Great Britain and Ireland is offering a Moynihan Prize in 1963 for the best dissertation or essay on a subject of the candidate's own choice relating to malignant disease.

The Prize will consist of a money award of £100, together with a medal. If, in the opinion of the Council, the subject-matter of an essay reveals facts which call for further research, the Council will consider making a grant for one year to help towards this end. The conditions of this grant shall be determined after consultation between the applicant and the Council. The Council reserve the right not to make an award in any one year.

The essay must be typewritten in English on quarto paper and bound. In assessing the merit of the dissertations, originality both in experimental and clinical observation will be regarded as being of the highest importance.

Essays submitted for the 1963 Prize must be received by the Honorary Secretary of the Association not later than December 31, 1962, and the award will be announced at the following Ceneral Meeting of the Association of Surgeons.

Each essay must be distinguished by a motto or device and accompanied by a sealed envelope containing the name and address of the author and having on its outside the corresponding motto or device.

Competition for the Moynihan Prize is open to men and women who are members either of the British Commonwealth or of the Republic of Ireland, who qualified not earlier than January 1, 1953, and who are either engaged in the practice of surgery or are being trained to this end.

The prize essay shall become the property of the Association of Surgeons, and, if the author desires publication, the essay must be submitted in the first place to the Editor of the *British Journal of Surgery*.

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